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CESAREAN SECTION IN MASSACHUSETTS IN 1939*

ROBERT L. DENORMANDIE, M.D.

BOSTON

THE following report on cesarean sections performed in Massachusetts in 1939 is the third in the five-year study.† Three additional questions were included in the questionnaire this year — the name of the consultant, the name of the operator and the birth weight of the baby.

The questionnaires were sent to one hundred and seventy-two licensed maternity hospitals, and replies were received from all but two. One hospital had been closed, and the records were not available. How many cesarean sections were done in this hospital is not known. It was found, however, that in 1 cesarean section done there the patient died after transfer to another hospital. The other that did not reply was a small hospital that had changed ownership. Its records were not available. In forty-two small hospitals, no cesarean sections were performed.

* * *

In Massachusetts in 1939 there were 62,575 live births and 1765 stillbirths, a total of 64,340. Of these, 52,697 were reported to us as having occurred in hospitals. There were 1984 cesarean sections performed and 12 hysterotomies, a total of 1996 abdominal deliveries, or an incidence of 1 in 32.2, compared with 1 in 30.3 in 1937 and 1 in 28.7 in 1938.

Table 1 gives a summary of the abdominal deliveries. The only significant change in this table is the marked increase in the number of sections of the extraperitoneal type. There were 20 in 1937 and 14 in 1938, compared with 34 in 1939. The reason for this increase is the new operative technic developed by Dr. Waters. There were 31 cases of the Waters type, 1 of peritoneal exclusion and only 2 of the Latzko type.

A short analysis of these 34 cases is interesting. Of the 31 patients on whom the Waters operation was performed, 17 made uneventful recoveries. Of these, however, 4 were not in labor, nor were the membranes ruptured; the operators obviously wished to try out the new technic. Of the 13 remaining cases of uneventful recovery, 7 patients had unruptured membranes, and 4 of these were in labor only eight to fourteen hours. The remaining 3 had labors of twenty-five, forty-eight and seventy-two hours. Of the 6 patients with ruptured membranes, 4 were in labor twenty-eight to thirty-six hours, with membranes ruptured from ten to thirty-two hours. One was in labor thirteen hours, with membranes ruptured twelve hours, and at operation a large hydrocephalic baby weighing 11 pounds, 5 ounces was delivered. In the last case in this group, forceps delivery was attempted twice but failed. This case I shall discuss later.

In the remaining 17 cases with the extraperitoneal type of operation, 2 patients died, and the others were reported as having had febrile convalescences. This group includes the 2 Latzko operations, the peritoneal exclusion and 12 of the Waters type. The answers to the questionnaires do not give the complete picture of these cases, and it is not fair to comment too harshly without

TABLE 1. *Summary of Abdominal Deliveries.*

OPERATION		NO. OF CASES
Cesarean section		1984
Emergency	921	
Elective	1059	
Not reported	4	
Type of operation:		
Low	1003	
Classic	898	
Latzko or extraperitoneal	33	
Peritoneal exclusion	1	
Porro	26	
Not reported	23	
In labor	616	
Not in labor	1302	
Not reported	66	
Membranes ruptured	313	
Membranes unruptured	1600	
Not reported	71	
Hysterotomy		12
Total		1996

*Read before the Fall River Medical Society, January 28, 1941, and before the Boston Obstetrical Society, February 18, 1941.

†The other two were published in the December 1, 1938, and July 11, 1940, issues of the *New England Journal of Medicine*.

further study. I record the summary of the analysis. The 2 patients that died, both following Waters operations, I shall refer to later under maternal deaths.

One patient on whom a Latzko operation was performed was in labor for thirty-six hours, with membranes ruptured for forty-eight hours. She is reported to have had a temperature on entrance to the hospital. She had a stormy convalescence, with a fever during her entire stay in the hospital, and was finally discharged from the hospital with a draining wound. The other patient on whom a Latzko operation was done was in labor, with ruptured membranes for eighteen hours. She had distention and fever for some days, but was discharged well. Both babies were discharged well. At birth they weighed respectively 7 pounds, 2 ounces, and 6 pounds, 14 ounces.

In the peritoneal exclusion case, the patient was in labor sixteen hours, with ruptured membranes ten hours. The baby was presenting by the breech and was delivered alive. The only note made on this case was that the convalescence was febrile.

The 12 cases of the Waters type of section that had febrile puerperiums remain to be analyzed. Two patients were not in labor, and the membranes were not ruptured. Of the remaining 10, 4 were in labor from twelve to twenty-three hours, and 6 from twenty-four to forty-eight hours. Of these 10 cases, in 1 the membranes were not ruptured, in 1 they were ruptured less than eleven hours, in 5 from twelve to twenty-three hours, in 2 from twenty-four to forty-seven hours, and in 1 forty-eight hours. The type of labor is not recorded in all, but in several it was noted to be only fair or poor, and in a few it was reported to have been hard.

The following complications were reported as occurring in these 12 patients. Two developed bronchopneumonia, and 1 a so-called "upper respiratory infection." Three developed pyelitis. One was reported as having septicemia, pneumonia, pulmonary embolus and empyema, and was transfused twice. Another was reported as septic, developing a pelvic phlebitis, pyelitis and embolus, and was twice transfused. Another, reported as having a febrile puerperium with endometritis, had an embolus. One is reported as having had a stormy convalescence, which was never serious. The 2 final cases were simply reported as septic. In this group, all the babies lived.

The number of Porro operations performed—26—is approximately the same as that in the two previous reports. Two of the 26 patients died. There is no need to analyze all the indications for these Porro operations, since they will be taken up later under the various indications for operation. There are, however, several that should be commented on here, because they might otherwise be overlooked. In 4 cases no recorded indication is given in the questionnaires. In 1 of these cases a Porro operation was done after a twelve-hour test of labor with a breech presenting. The baby weighed 6 pounds, 8 ounces. Two other cases were repeat elective sections. The fourth operation was done on a forty-four-year-old primipara following a twelve-hour labor, and a contraction ring was found. The baby in this case was stillborn. A thin scar of a previous section was the recorded indication for 1. In 1 case a branch of the uterine artery was torn at the cesarean section, and a Porro operation was done at once. In another case, an elective repeat section, the uterus continued to bleed, and a Porro was thought to be indicated. The baby in this case weighed but 5 pounds.

TABLE 2. *Indications for Hysterotomy.*

INDICATION	NO. OF CASES
Cardiac disease	5
Hypertension	2
Nephritis	1
Manic-depressive insanity	2
Hereditary chorea	1
Increasing toxemia	1
Total	12

The final case in this group on which I wish to comment is that of a patient with membranes ruptured fourteen hours, in labor twelve hours. It is recorded that free pus was found in the uterus, yet the patient made an afebrile convalescence. The baby weighed 11 pounds, 8 ounces, and died on the eighth day. At autopsy both kidneys showed free pus.

Table 2 shows the indications for the 12 hysterotomies. These are clear, and no comment is necessary.

TABLE 3. *Types of Anesthesia.*

ANESTHETIC	NO. OF CASES
Nitrous oxide, oxygen and ether	1255
Ether	194
Cyclopropane	136
Spinal	185
Nitrous oxide and oxygen	18
Avertin, and nitrous oxide, oxygen and ether	29
Local	22
Other	135
Not reported	10
Total	1984

Table 3 records the types of anesthesia. The use of spinal anesthesia has increased slightly, and the use of cyclopropane has dropped. The others remain in relatively the same proportion. Un-

der the heading "Other" are grouped various combinations that were used and some of the newer anesthetics. Two deaths apparently must be assigned to anesthesia, and they will be reported under the maternal deaths.

Table 4 shows the reported indications for operation in cases in which the baby died. Although

TABLE 4. *Indications for Operation in Cases with Death of the Baby.*

INDICATION	EMERGENCY CESAREAN SECTION	ELECTIVE CESAREAN SECTION
Separated placenta	33	1
Placenta previa	42	3
Toxemia and nephritis	5	7
Previous cesarean section	10	22
Prolonged labor	3	–
Contracted pelvis	1	2
Ruptured uterus	2	–
Previous operative attempts	3	–
Desire of patient	–	1
Eclampsia	3	–
Test of labor	5	–
Previous disaster	1	2
Cardiac disease	1	2
Pyelitis	–	1
Diabetes	–	2
Amputation of cervix	–	1
Malposition	2	–
Hydrocephalus	2	–
Anencephalus by x-ray	–	1
Hydramnios	–	1
Elderly primipara	1	–
Disproportion	3	–
Breech	1	–
Tonic uterus	1	–
Surgical emergency	1	–
Bizarre	3	–
Obstructing tumor	–	1
Not reported	1	2
Totals	124	49

the actual number of babies lost is lower, the percentage is slightly higher than that in 1938.

It is difficult to tell from the questionnaires in how many of these sections the first two indications in Table 4 were for the best interests of the patients. Undoubtedly many were questionable, for some were done at five or six months' gestation, and in many of the previas the babies' weight was reported to be 4 pounds or less. One such patient, on whom a Porro was done, is reported as having moderate bleeding at six months.

Under "Toxemia and nephritis," 12 babies were lost. There is always a serious risk to the babies in these cases, and the loss of 12 is not surprising. It is only by careful prenatal care that the number and severity of the toxemias can be reduced, and so long as such care is not given deaths from this cause will continue.

Thirty-two babies were lost following cesarean section done because of a previous section. Of the 10 classified under "Emergency," 3 were lost because of ruptured uteri, 3 because of premature labor, — the babies weighing less than 5 pounds, — 2 because of separated placentas, — 1 of these babies being macerated, — 1 because of erythroblastosis and 1 because of alleged congenital heart disease, although no autopsy was performed.

In the elective repeat sections, 22 babies were lost. The cause of 7 of these deaths was atelectasis or prematurity; 4 infants had malformations incompatible with life; 2 died from erythroblastosis; 2 died from toxemia; 2 were stillborn, 1 of these being macerated; 1 each died from hemorrhagic disease of the newborn, cerebral hemorrhage and congenital heart disease; and 2 died from complications arising after birth, 1 from abscess of the lung and 1 from bronchopneumonia.

It is obvious that some of these deaths were unavoidable, but unless all the 32 original cesarean sections were necessary, through the repeat sections the patients were subjected to an operative procedure that failed to give a living baby.

It is difficult to explain why the babies were lost in many of the elective sections. It seems hardly reasonable to perform a section on a known malformed fetus, and it is a doubtful procedure on a patient presenting hydramnios.

As in the elective sections, some of the emergency deaths were unavoidable. But the loss of so many babies shows conclusively that the choice of a cesarean section in some cases was, to say the least, questionable. It must be recorded that in 4 of the emergency sections the fetus was macerated. Reasonably good judgment was lacking.

Table 5 shows the indications given for operation. It is arranged approximately as that in the other reports.

There is no need to comment on each indication. Contracted pelvis and disproportion total 336. Of these, 179 were classified as contracted pelvis. One hundred and thirty-seven of the 179 patients had no labor. One baby weighed under 5 pounds, 14 under 6 pounds, 51 under 7 pounds and 61 under 8 pounds — a total of 127 babies of average size. One woman said to have had a large baby was operated on and delivered of twins. There were 39 babies weighing over 8 pounds, and 12 cases in which the birth weight was not recorded. One hundred and fifty-seven cases are classified under "Disproportion." Seventy-four of these had no labor, and a section was done presumably because the operators regarded the babies as too large for a normal delivery from below. Analysis of the weights of the babies shows 2 under 5 pounds, 2 under 6, 21 under 7 and 57 under 8 pounds. Seventy babies weighed 8 pounds or over, and in 5 cases the birth weight was unrecorded.

Under the indication "Contracted pelvis," 82 cesarean sections were done without consultation, but under "Disproportion," there were only 40.

Farther down in the list of indications, 164 cases are classified under "Test of labor." In these, 1 baby weighed under 4 pounds, 1 under 5, 4 under 6, 23 under 7 and 47 under 8 pounds. There were 74 weighing 8 pounds or over, and in 14 cases the weight was not reported.

If the number of babies weighing under 7 pounds in these 3 indications are added together, the total is 120, or 24 per cent of the 500 cesarean sections labor under twelve hours, 2 from twelve to twenty-three hours, 13 from twenty-four to forty-seven hours, 3 from forty-eight to seventy-two hours, and in 2 the length of labor was not reported. In this group, 4 babies were lost and there was 1 hydrocephalic case. Six of these women developed severe puerperal sepsis, but all, fortunately, recovered. Seven of the babies weighed under 7 pounds, and 1 of these was under 6. Several of the babies

TABLE 5. *Indications for Cesarean Section.*

INDICATION		NO. OF CASES
Previous section		608
Contracted pelvis and disproportion		336
Placenta previa		215
Separated placenta		86
Toxemia		78
Eclampsia		11
Malposition of baby		79
Breech	50	
Transverse	21	
Brow	2	
Face	6	
Dystocia		220
Dystocia	9	
Labor without progress	23	
Test of labor	164	
Cervical dystocia	24	
Previous surgical operations		36
Repair of perineum	13	
Amputation of cervix	9	
Repair of cervix	5	
Myomectomy	4	
Pelvic surgery	3	
Repair of fistula	2	
Associated medical conditions		51
Cardiac disease	24	
Tuberculosis	2	
Diabetes	16	
Multiple sclerosis	1	
Pyelitis	2	
Chronic nephritis	6	
Previous obstetric disaster		52
Elderly primipara		58
Obstructing tumors (fibroids)		24
Fetal distress		6
Prolapsed cord		4
Following operative attempts		7
By request or for sterilization		10
Request	9	
Sterilization	1	
Ruptured uterus		8
Spontaneous	2	
Previous section	6	
Bicornate uterus		1
Postmaturity		3
Malformation of fetus		4
Malformation of vagina		1
Error in diagnosis		1
Surgical emergency		1
Bizarre		32
Not reported		52
Total		1984

performed. But the total number of babies under 8 pounds is 285, or 57 per cent of the number of sections done for these three indications. There can be but one conclusion from these figures: that a large number of the sections are totally unjustified.

I have already spoken about the questionable procedure of performing sections on some of the patients with placenta previas and separated placentas.

There has been a marked drop this year in the number of sections for toxemia, but the number for eclampsia remains about the same. In the 11 cases of eclampsia, 2 mothers and 3 babies died.

Under the indication "Dystocia," there were 9 cases. In 1, labor was mild, and the length was not reported. The other 8 had labors of from thirty-four to seventy-two hours. Two cesarean sections were by the Waters technic, and the others were of the low type. All the babies were discharged well. Five of these patients had febrile puerperiums and for a time gave considerable worry to the operators.

There are 23 cases under "Labor without progress." Two patients were reported as having that died were not weighed. It is well to note here that all babies should be weighed, whether they are born alive or dead, for comparison in future deliveries.

Twenty-four cases are classified under "Cervical dystocia." In 1 the operation was done before labor began, because of a badly scarred and lacerated cervix. A second was done after eight hours of labor for "cervical atresia." Two of the patients in this group were in labor for two days, 2 for three days and 1 for four days, but the significant remark was made in this questionnaire that the patient had "several bouts of false labor during this time." All the other patients were in labor from eighteen to twenty-four hours, except in 4 cases in which the length of labor was not reported. In 15 cases the membranes were not ruptured. Six of these patients had a febrile puerperium. All the babies were born alive. Six weighed under 7 pounds, and 1 weighed only 3 pounds, 13 ounces. One mother died, and this case will be discussed later.

No comments are necessary on the 36 cases classified under "Previous surgical operations," except to note that following an amputation of

the cervix the section should, if possible, be an elective and not an emergency one.

Under "Associated medical conditions" there are 51 cases. It is an interesting fact that because of the control of diabetes by the use of insulin, the number of diabetic patients who become pregnant is increasing. All the mothers and all but 2 babies in this group lived.

No babies died under the indications "Fetal distress" and "Prolapsed cord." In 2 of the latter cases the prolapsed cord was in the first of twins. In 1 of these cases the mother had an extremely stormy convalescence, was septic, developed a phlebitis, but eventually recovered.

In 1 case of "Fetal distress," it was noted that the mother had no labor but that the fetal heart was slow. A section was done, and a baby weighing 5 pounds, 8 ounces was delivered. The heart continued slow, and a diagnosis of congenital heart block is recorded.

Again I regret having to report cesarean sections done following operative attempts at delivery from below. At best it is a dangerous procedure, and should not be attempted unless the previous operative attempts have been made with most meticulous care. The seriousness of this procedure is demonstrated by the fact that 4 mothers and 3 babies died in cases in which operative attempts had failed. The maternal deaths I shall report later in this paper. There is 1 case, however, on which I wish to comment, not as an illustration of good obstetrics but of good luck. After two days of slow, irregular labor, the patient became fully dilated. The head remained high. A forceps was applied by the house officer without success. The visiting surgeon was sent for, and the note on the questionnaire says, "With considerable amount of pull, no give for him. Therefore a cesarean was decided on." It is recorded that a Waters type of section was done, and the patient made an uneventful convalescence, the baby weighing 9 pounds, 7 ounces.

Regarding the indication "By request or for sterilization," I can only repeat what I have said so many times before: that to me it is utterly unjustifiable to do a cesarean section simply at the request of the patient or only to sterilize. In 1 section done at the patient's request, the baby was lost. The surgeon who operated must have found it difficult to justify such an operation with the loss of the baby.

Under "Ruptured uterus," 2 spontaneous ruptures were reported and 6 cases in which previous sections had been done. All the mothers lived, and 3 babies were born alive. One of these patients had had a longitudinal low-flap section in the first pregnancy, followed by two normal deliveries. In this, the fourth pregnancy, rupture occurred after twenty-four hours of labor, the baby weighing only 5 pounds.

Another interesting case in this group is that of a patient admitted to a hospital in shock. The operator writes:

> The ovum was found to be completely in the abdominal cavity and the uterus well shut down with a rupture extending from the left cornu to the region of the cervix on the right side. There was a good deal of amniotic fluid in the sac, which was opened to extract a dead baby. The tear in the uterus was repaired and a drain placed to the pelvis. The patient made an uneventful recovery. She later returned for sterilization.

This case is classified as a spontaneous rupture. The patient had been in labor for two or three days, and had been etherized, but it was reported that she had not been operated on.

Under the indication "Postmature," there is only 1 case on which I wish to comment. The questionnaire states, "Head not in the pelvis, overdue two weeks." A section was done without a consultation, and a baby weighing 5 pounds, 8 ounces, was delivered.

The indication for 4 sections is given as "Malformation of the fetus." Three were hydrocephalic, and 1 was anencephalic. This does not mean that these were the only malformed babies in this series; others occurred, but the malformation was not the primary cause for the section, as in these 4 cases.

Two of these cases, it is recorded, had x-ray examinations. In 1 case the baby weighed 5 pounds, 8 ounces, and as it was being delivered through the incision the head collapsed. The notes on the second case say that "the patient had two premature births at five and six months, and both children died. In view of the x-ray findings and a very large child, it was thought best to do a cesarean section." The weight of this anencephalic monster is not given. In 1 case the baby weighed 11 pounds, 5 ounces, but it is not recorded that an x-ray film was taken. The final case also has no record of an x-ray examination. The baby weighed 7 pounds, 8 ounces, and the patient was operated on after, it is said, three days of labor. She had a pulmonary embolus, which eventually cleared up.

The 1 case of "Error in diagnosis" was that of a general surgeon operating for a large ovarian cyst.

The "Surgical emergency" was the case of a woman brought to the hospital *in extremis*. The abdomen was opened, and pus poured out. The patient had had no previous medical care. The baby was stillborn, and the mother died on the table.

Thirty-two sections were for indications clas-

sified as "Bizarre." I shall not attempt to enumerate each of these indications, but I do wish to mention a few: "A highly resistant luetic"; "distinct endocrine type"; "severe pain in the right lower quadrant"; "undilatable soft parts" (this patient was not in labor, a cesarean was done, and the baby weighed 5 pounds, 14 ounces); "interlocking twins"; "multiparity." Three sections were done for so-called "dystocia," yet 2 patients had no labor and 1 had labor for only four hours, and the babies weighed respectively 6 pounds, 2 ounces, 5 pounds, 1 ounce, and 7 pounds, 2 ounces. There were 2 cases of cervical dystocia, but the patients had no labor. One baby weighed 6 pounds, 15 ounces, and the other eight pounds. These 2 cesarean sections were done by the same surgeon. It is obvious that he wanted to do a section on the patients. There is no recorded adequate indication. Three patients were said to have a floating head, and were not in labor. One indication was "primary inertia with torsion of the uterus." There was no labor. In a final case the patient was said to have had a previous dystocia in her first labor, but did not go into labor this time. A 6-pound baby was delivered.

TABLE 6. *Summary of 54 Cases with Maternal Death.*

DATA	NO. OF CASES
Emergency operation	45
Elective operation	9
Type of operation:	
Low	24
Classic	26
Porro	2
Waters	2
In labor	29
Not in labor	25
Membranes ruptured	15
Membranes unruptured	39
Babies:	
Living	42
Dead	12

It is reported that 68 patients were sterilized at the time of the section.

Table 6 presents a summary of the 54 cases with maternal death. It needs no comment.

In Figures 1 and 2 the data on the maternal deaths are presented in the same manner as in 1938. Figure 1 analyzes the 9 elective sections, and Figure 2 the 45 emergency operations in which death occurred. Some of these cases have already been remarked on. Others need no analysis.

For 1939 there was an encouraging drop in the number of deaths following elective section, only 9 cases being so classified.

Of the 4 deaths giving sepsis as the cause of death, the indication was "contracted pelvis" or "disproportion" in 3 and "repeat section" in 1. This last patient was prepared for operation one morning, but the membranes ruptured during the night and a section was done within an hour.

One patient had a hard operative delivery with the first baby and a large baby in the present pregnancy. She was sterilized following the cesarean section, and the appendix was removed. The operator, a general surgeon, did not ask for a consultation. In this case the sepsis may have originated from the appendectomy. It is a possible cause, and therefore this operation at the time of a cesarean section is always contraindicated.

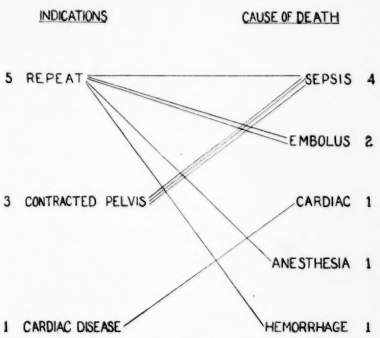

FIGURE 1. *Maternal Deaths in 9 Elective Cesarean Sections.*

The third patient was a dwarf with a contracted pelvis. On entrance to the hospital it is reported that she had a temperature of 101°F., with a negative physical examination. Distention occurred in twenty-four hours. The temperature and pulse continued to rise, and the patient died on the morning of the fifth day. The death certificate gave "paralytic ileus" as the cause.

In the final case of sepsis, a staphylococcal bacteremia, section was performed because of a "pelvic outlet smaller than the average." The baby weighed 6 pounds, 13 ounces.

The 2 deaths from embolus were in repeat sections, one occurring on the sixth day and the other as the patient was being helped up the steps to her home on the eleventh day.

The cardiac patient was decompensated, was operated on under local anesthesia, grew steadily worse, and died on the sixth day.

The death assigned to anesthesia occurred in a repeat section. The patient took the anesthetic poorly and had to be resuscitated in the middle of the operation. Twelve hours after operation she developed considerable distention, with a temperature of 102°F. Distention increased, the tem-

perature ranging about 103°F.; she died on the sixth day. The death certificate gave bronchopneumonia as the cause of death.

The final death following elective cesarean section occurred in a repeat section three hours after operation. The cause of death on the certificate was "surgical shock, embolus." When the operator attempted to remove the placenta it was found to be an accreta. The patient bled profusely, and a Porro operation was done immediately. Salt solution was given subpectorally at once. While preparations were being completed for

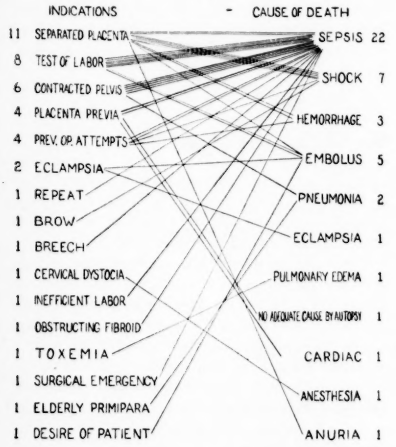

FIGURE 2. *Maternal Deaths in 45 Emergency Cesarean Sections.*

transfusion, the patient died. In this case there was a delay of at least two hours in transfusing. Had this patient been transfused promptly, her life might have been saved.

Forty-five patients died following emergency sections. In these cases, 22 deaths were assigned to sepsis. Fourteen were so designated by their physicians on the death certificate.

One of these cases I report in detail. The patient was a thirty-year-old primipara in labor some forty-five hours, with membranes ruptured an unknown number of hours. Dilatation was very slow. Two vaginal examinations were made. A section was finally decided on. The temperature was reported as 102.6°F. Before the section, of the classic type, was done by a general surgeon, a low pressure 5-gallon douche was given. After the operation, the patient showed signs of sepsis, and in spite of intravenous fluids, sulfanilamide and a transfusion, died on the seventh day.

The other 8 cases, not so designated by their physicians, I have placed under sepsis because of the history that was obtained in the maternal mortality study, and they may need explanation. In 4 cases the cause given on the certificate was "paralytic ileus," with or without toxic or acute myocarditis, and in 1 case the cause given was "acute dilatation of the stomach." There can be no question that these 5 deaths should be attributed to sepsis. In 1 case the certificate gave "uremia" as the cause of death. The patient did have suppression of the urine, but she also was septic. Another case gave "toxemia and hemorrhage following a separated placenta" as the cause of death, but from the interview with the physician and from the hospital record the death was definitely thought by the investigator to have been caused by sepsis. In the final case the cause of death on the certificate was "right lobar pneumonia." The evidence in this case is not conclusive, but the facts as brought out by the study are these: After seventeen hours of labor, the cervix being dilated to admit three fingers, a version was attempted on a hydrocephalic baby. It was unsuccessful. One hour later the patient was again etherized, and again the version failed. At this time a ruptured uterus was suspected. The temperature was found to be 104°F., the pulse 140. The patient was then etherized a third time, and a Porro was done because of this ruptured uterus. Death occurred fifty-two hours after operation. There was a suggestion that the patient had an upper respiratory infection on entrance to the hospital, but no temperature was recorded on the questionnaire. She may have died of pneumonia, but I have assigned the death to sepsis. No matter to what cause the death is attributed, it was the result of bad obstetrics.

Of the 7 deaths from shock, 5 followed separated placenta. In 1 of these cases there was a delay of four hours in getting the patient to the hospital, a distance of ten miles, because of a very heavy snowstorm at the time. Two cases of shock followed failure of previous operative attempts.

In the 3 deaths assigned to hemorrhage, 2 followed operations because of separated placenta, and in 1 a cesarean section was done after operative attempts at delivery from below had failed. In 1 of the first 2 cases the patient oozed from a pinprick of the ear, and from a vein where a transfusion was done. Two of these deaths from post-partum hemorrhage occurred in the same hospital two to four hours after operation and raise

the question whether the nursing care in these cases was adequate. Should they be regarded as preventable deaths?

Two of the patients whose deaths were assigned to embolus ran septic temperatures (1 following a Waters type of cesarean) for over a week, and from the questionnaires one wonders whether they were not allowed up too early. It is to be noted that in 1 death assigned to embolus the indication was "the wish of the patient."

The deaths assigned to pneumonia and eclampsia need no comment.

The case attributed to pulmonary edema occurred in a primipara with toxemia. She was in labor some twenty hours, and by the hospital record fully dilated for five hours when a cesarean section (Waters type) was done. At the operation the patient bled more than an average amount. Following operation she passed bloody urine, and twelve hours postoperative the temperature was 102°F., the pulse 140, and the blood pressure 186 systolic, 80 diastolic. Twelve hours later she suddenly developed pulmonary edema and died.

The next death was that of a patient operated on for placenta previa. The note from the obstetrician who investigated this death states that the post-mortem examination, which was performed by a capable pathologist in the presence of several clinical observers, completely failed to reveal the cause of death. The proper diagnosis remains "unknown."

The cardiac death occurred in a woman with long-standing cardiac disease in her tenth pregnancy. She was admitted to the hospital in the seventh month, with partial decompensation. While in the hospital under treatment she began to bleed from a placenta previa. A section under nitrous oxide, oxygen and ether anesthesia was done at once. The baby, weighing nearly 5 pounds, lived, but the mother died on the second day.

The death assigned to anesthesia occurred in a patient who weighed 240 pounds. She had been in labor twenty-four hours. The anesthetist tried for an hour and ten minutes to anesthetize her with nitrous oxide and oxygen. Failing in this, she was given Epival intravenously, and a low section was done at once. The temperature immediately rose to 102°F., with respirations of 40 and rales throughout the chest. She became very dyspneic and cyanotic, and died on the second day.

The last patient in this group had had eclampsia with her first pregnancy and a separated placenta with the third, in both of which cesarean sections had been performed. She had a separated placenta with this, the fourth, pregnancy. The systolic blood pressure before operation was 220. The patient passed no urine for four days, and died on the seventh day.

* * *

This report shows an encouraging drop in the number of cesarean sections performed in 1939, but it also demonstrates conclusively that too many sections are still being done in Massachusetts.

Cesarean sections figured in 21 per cent of the total number of maternal deaths, demonstrating that this procedure is a major cause of keeping up maternal mortality in the State.

One thousand and ninety consultations are reported, but the consultation in many cases was the mere formality of having a surgeon see the case before he operated.

In some communities a trained obstetrician is not available to lend aid in difficult problems, and the physicians turn to surgeons for help in what appears to them to be serious situations. Few of these surgeons have had any training in obstetrics. They know how to do nothing in the obstetric field, yet do not hesitate to subject a woman to what in many cases is an unnecessary operation.

There are relatively few patients who cannot have the advantage of a really valuable consultation if their physicians give them adequate prenatal care. In most cases, cesarean section should not be an emergency operation, and therefore if a physician wishes and has the best interests of his patients at heart he can always obtain competent help, and need not rely in an emergency on an untrained surgeon who is willing to cut without any desire to think.

One hundred and seventy-three babies were lost. This total is too large and must be lowered if our results are to be regarded as satisfactory. Careful evaluation of the proper method of delivery was not present in many cases. To subject a woman to a section when the baby has a known malformation incompatible with life is not good obstetrics and is not demanded by any religious dogma. Such indications must be eliminated.

Sepsis, as we all know, has been the major cause of deaths from cesarean section, and 1939 was no different from any other year. That 50 per cent of the deaths should be from this cause is a serious criticism of the operators, and as I have said before, these operators must revise both their technic and their judgment in choice of operation. In neither of these points can they be regarded as suitable operators unless marked improvement is shown.

On many previous occasions I have called attention to the fact that the deaths following cesarean section are scattered; no one operator has

several. For 1939, twenty-six hospitals reported 1 death each, nine 2, two 3, and one 4. In the last hospital 31 cesarean sections were performed, and in 2, death followed post-partum hemorrhage. Such a result is a serious criticism of the hospital, and the cause should be studied and speedily rectified.

The variation in the incidence of cesarean section in large clinics is interesting. How much criticism one can justifiably make is uncertain, but the facts are undeniable. In the two largest clinics in the State the respective incidences were 1 in 36 and 1 in 33, whereas in two other hospitals in the same city the respective incidences were 1 in 11 and 1 in 17. The four largest clinics in another city show respective incidences of 1 in 48, 1 in 40, 1 in 28 and 1 in 19. The complete story is not told by the questionnaires, but one fact is obvious: the major difference in the incidence occurs when private patients are included in the total figures.

The committee appreciates the co-operation shown by practically all the hospitals in filling out the questionnaires. There was, however, a great variation in the care shown in the answers. The large majority of hospitals filled out the questionnaires fully and carefully, but in a few, usually the smaller ones, the answers were not always satisfactory. In one proprietary hospital in Boston no indication was given for any cesarean section done. In another hospital, no records were filled out for one physician's private cases.

The replies to the questions concerning consultant and operator were so incomplete that no attempt was made to draw definite conclusions. It is clear, however, that in many cases a general surgeon operated, and that no adequate consultation was held.

In many of the hospitals the rule of the American College of Surgeons that all major obstetric operations call for a consultation is being enforced, but not in all. In some hospitals the physicians are graded in relation to what they are allowed to do, and this obviously is a step in the right direction. Until this is done in all hospitals, whether it be in surgery or obstetrics, poor results will continue.

330 Dartmouth Street

TUBERCULOSIS AND MOBILIZATION*

FREDERICK T. LORD, M.D.†

BOSTON

VOLUNTARY tuberculosis associations throughout the United States have a responsibility in connection with mobilization to urge the exclusion of tuberculous men from the Army, and to help in every way possible in the follow-up of those rejected because of the disease. Adamson[1] reports that the Defense Department of the Dominion of Canada has ordered a chest x-ray examination of every recruit. Standard films and technic have been used. The percentage of rejections for tuberculosis have amounted to 1.06.

Tuberculosis and Mobilization, 1917–1918

In 1917 and 1918, under the selective-service regulations, reliance was placed on physical signs for the exclusion of pulmonary tuberculosis. No mention was made of the use of x-ray films in this connection, but registrants were at times thus examined by medical advisory boards. I was at that time a member of an advisory board and placed much more confidence in physical signs for the discovery of pulmonary tuberculosis than I do now, and called for an x-ray examination only in selected cases.

The selection of registrants for service in 1917–1918 was made under pressure in the face of an emergency. Many men with tuberculosis entered the service, and the magnitude of the tuberculosis problem in disabled veterans may be judged by the cost, which for hospital care, insurance benefit in excess of paid-in premiums, vocational training and compensation, is estimated by Spillman[2] to have amounted already to approximately $960,000,000.

The tuberculosis problem was much more serious in the United States then than it is today. In Massachusetts, for example, the death rate from the pulmonary form of the disease in 1917 was 121, and in 1940 it had fallen to 34 per 100,000 population.

Tuberculosis and Mobilization, 1940–1941

In spite of the remarkable decline in tuberculosis, the pulmonary form is still a serious menace, and more persons in the selective-service age group in Massachusetts succumb to tuberculosis than to any other single cause.

*The President's Address, delivered at the annual meeting of the Massachusetts Tuberculosis League, Boston, March 20, 1941.

†Clinical professor of medicine, emeritus, Harvard Medical School; member, Board of Consultation, Massachusetts General Hospital.

Examination for physical fitness for service of 6,000,000 of the 16,000,000 registrants offers an unusual opportunity for tuberculosis case finding and control on a large scale. It should eliminate those unfit for service from this cause, and through discovery and treatment should safeguard the health of the individual and protect his family and the community.

Once a man is in the service, there is the likelihood of activation of the tuberculosis under physical effort, and danger of spread of the disease to others in the close contact of soldiers in barracks and tents and at mess. Furthermore, the classification of pulmonary tuberculosis in military personnel as occurring in line of duty can be made with fairness only when an x-ray examination, in addition to other methods of investigation, has been made before induction and those with the disease have been rejected.

The expected rejections for tuberculosis among selective-service registrants in the United States may be roughly estimated from the 1.06 per cent rejected for this reason in Canada. There the death rate from the disease is 54.7 (Adamson[1]). For the year 1939 in the United States, the death rate from tuberculosis was 46.6, suggesting that with methods similar to those used in Canada the rejections here would in general amount to slightly less than 1 per cent. Since the death rate from this cause varies from 191.0 in Arizona to 15.8 in Nebraska, the percentage will differ in the various states. There are, in addition, some doubtfully significant or suspicious lesions that should later be re-examined. Among other disturbances to be expected, in rare cases, are cysts, polycystic disease, bronchial, pulmonary and mediastinal neoplasms, fibrosis, nontuberculous pneumonia and eventration of the diaphragm.

Importance of X-ray Examination

In the diagnosis of pulmonary tuberculosis, the history is important, and the physical examination should not be neglected. Progress in x-ray equipment and technic, however, is such that no examiner, however skillful, can compete with it in obtaining evidence in difficult cases for the exclusion of those with the disease.

In the use of the x-ray examination of registrants, greater reliance should be placed on standard large (14-by-17 inches) than on miniature films. Competent roentgenologists and facilities for the x-ray examination of registrants are available, and the expense involved is insignificant compared with the cost and hazard incident to admission of those with the disease into service.

In the selection of registrants for service during mobilization, examining physicians are cautioned to be extremely careful to reject those with pulmonary tuberculosis. In the official regulations[3] it is stated, "The chest examination will include the usual methods of physical diagnosis, *supplemented, whenever indicated, by radiographic* and laboratory studies* [italics mine]."

Inadequacy of the Present Program

Routine x-ray examination of the lungs of registrants is not required before induction. The lack of general appreciation of the importance of the roentgenogram means that pulmonary tuberculosis has not been excluded in a large proportion of the men called up for service in the United States.

In the First Corps Area (including Maine, New Hampshire, Vermont, Massachusetts, Rhode Island and Connecticut), through the co-operation of the New Hampshire Tuberculosis Association, the New Hampshire Department of Health, the Adjutant General and the federal military authorities, New Hampshire has led the way in the x-ray examination of men called into service, Burroughs and Frechette[4] reporting that between September 16 and 26 all officers and enlisted men of the National Guard and candidates for enlistment had an x-ray examination of the chest.

In Massachusetts, through the co-operation of the Massachusetts Department of Public Health and the Army Medical Corps, an x-ray examination has been made of most of the national guardsmen and of the selective-service registrants, when they appeared before the induction boards.

Throughout the First Corps Area the x-ray examination of men called up for service has been carried out in five of the states under the auspices of the state departments of health, assisted in New Hampshire and Vermont by the state tuberculosis associations. In Connecticut it has been carried out under the auspices of the State Tuberculosis Commission.

Not all members of the National Guard inducted into service had chest x-ray examinations, since some had already been inducted into service before the program was under way. In one state, sufficient funds were lacking. In another, chest x-ray studies were made only when it seemed necessary.

Selective-service registrants in the First Corps Area have had an x-ray examination at the time of their appearance before the induction boards. In two states, the x-ray films were developed and read on the day of induction. In one, some, but not all, of the films were interpreted before induction, and in three states none of the films were interpreted before enrollment into service.

From the experience in the New England states,

*X-ray machines, for use in connection with the photography of the fluorescent-screen image on a 4-by-5-inch film, have been ordered by the United States Army.

it is evident that the program has suffered from failure to make plans in advance of mobilization to include and provide funds for a chest x-ray examination as a routine, and to require that registrants be found free of pulmonary tuberculosis by this means before induction into service.

As a result of postponement of the x-ray examination until appearance before the induction boards, those rejected are likely already to have made plans for enrollment, and if there is delay in reporting positive x-ray findings on an otherwise qualified registrant, the man is already in service and may have to be recalled from some distant point.

Recommendations of the National Tuberculosis Association

At the meeting of the Board of Directors of the National Tuberculosis Association on February 15, concern was expressed regarding the lack of adequate provision for excluding pulmonary tuberculosis from the United States Army. A resolution was unanimously adopted that in the opinion of the board it is highly undesirable to induct men with pulmonary tuberculosis into the Army of the United States and that an x-ray examination of the chest is necessary to exclude the disease. The board makes an urgent appeal that all volunteers and prospective recruits be examined by this means and be found free of pulmonary tuberculosis before induction.

To accomplish this purpose, the orders should come from Washington, and arrangements should be made by local boards for x-ray study at the time of examination. If this study must be delayed until the registrant appears before the induction boards, enrollment into service should be postponed until the result of the x-ray examination is known.

305 Beacon Street

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PARATHYROID ADENOMA*

Report of Three Cases

ROBERT C. COCHRANE, M.D.†

BOSTON

THE following histories of three proved cases of parathyroid adenoma are presented as illustrating the symptoms, findings and some of the difficulties encountered in diagnosis, operation and postoperative treatment of this condition.

CASE REPORTS

CASE 1. L. O. (B. C. H. 657485, referred by Dr. Joseph H. Shortell), a 30-year-old woman, entered the hospital on December 16, 1931, complaining of a dull pain in the left thigh of several months' duration. She walked with a marked limp, and there was a tender area over the left sacroiliac joint.

X-ray examination showed an area of destruction in the outer aspect of the left ilium, and multiple areas in the right ischium and pubis. There were several punched-out areas in the skull and mandible. Similar punched-out areas, with irregularity of outline, were seen in both tibias, the left fibula and both humeri. The spine was normal.

A tentative diagnosis of multiple myeloma was made, but the pathological report on a biopsy from the left tibia showed a tumor of the giant-cell class; the suggestion was made to study the parathyroid function. The blood calcium at this time was 9 mg., and the phosphorus 2.2 mg. per 100 cc.

In February, 1932, after further x-ray studies, the diagnosis of osteitis fibrosa cystica was made, and Dr. Soma Weiss, with parathyroid dysfunction in mind, put the patient on a high-calcium diet, with viosterol in large doses. After 4 weeks, x-ray films showed marked bone regeneration in the previously rarefied areas of the pelvis. The patient was discharged from the hospital on a high-calcium diet, and an x-ray film the next month showed the defect in the right ilium to be entirely filled with solid bone.

She was readmitted to the hospital on May 13, because of a pathological fracture of the upper third of the left femur. The blood calcium was 13 mg. and the phosphorus 4.1 mg. per 100 cc. (Fig. 1). On June 14, her neck was explored and a search made for a parathyroid tumor. None was found, but two small masses thought to be parathyroid glands were removed. Only one of them proved to be parathyroid tissue. Following the operation the patient developed secondary anemia and sustained a pathologic fracture of the left humerus. The cortex of all the long bones at this time was almost paper thin (Fig. 2).

On July 7, a second exploration of the neck was made, and the left lobe of the thyroid gland was removed. No parathyroid tissue was found. The blood chemical find-

*Presented at the annual meeting of the New England Surgical Society, Poland Spring, Maine, September 28, 1940.

†Assistant professor of surgery, Harvard Medical School; surgeon-in-chief, second surgical service, Boston City Hospital.

ings remained unchanged. On August 4, the patient sustained a pathologic fracture of the right femur, and 2 weeks later, a pathologic fracture of the right humerus. By the middle of September, x-ray study showed union of all these fractures, save for a recent one of the second left metacarpal. She was seen in consultation by Dr. Frank H. Lahey, and it was agreed that her condition, which had become steadily worse, would not justify a third operation at that time.

By January, 1933, x-ray examination showed the presence of stones in both kidneys. The patient was discharged at her own request in August, with her general condition somewhat improved, and was to return for further exploration of her neck in September.

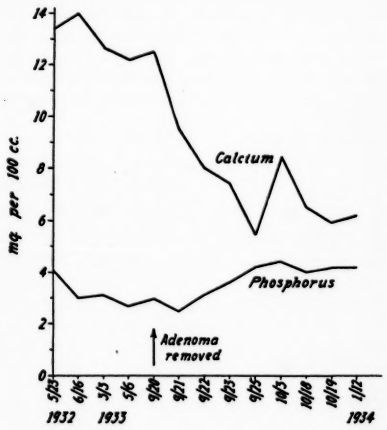

FIGURE 1. *Laboratory Data in Case 1.*

In the meantime she sustained another pathologic fracture of the left humerus and was readmitted to the hospital. She was again seen in consultation, and operation was decided on after Dr. Lahey had suggested the possibility of an intrathyroid parathyroid tumor. This third operation was done on September 20, at which time a parathyroid adenoma, the size of a lima bean, was enucleated from within the posterior portion of the right lobe of the thyroid gland. Twenty-four hours after the operation, the blood calcium was 9.5 and the phosphorus 2.5 mg. per 100 cc. The calcium continued to drop, and 4 days later was 5.4 mg., and never became higher than 6.5 mg. subsequently, in spite of much medication. The phosphorus on this day was 4.2 mg. and thereafter did not change. The patient developed a positive Chvostek sign 24 hours postoperatively, and in spite of being given parathormone three times daily, within a week she had developed a positive Trousseau sign and other signs of tetany. These disappeared within 4 days, with the exception of the Chvostek sign, which persisted for 2 weeks longer. Unfortunately, she then began to develop signs of kidney infection, and in spite of all measures, she became progressively worse, and died on February 18, 1934.

Post-mortem examination showed bilateral pyohydronephrosis, with stones in both kidneys and multiple abscesses, and generalized osteitis fibrosa cystica. No parathyroid tissue was found in the neck or substernally.

Comment. This patient was in the usual age and sex group. Her chief complaint was also typical, that is, dull pain in an extremity. She did not show a hypercalcemia at first, although the phosphorus was low. Four months later the calcium was high, but the phosphorus was normal. At the time of the first operation the blood chemical findings were typical, but extensive exploration failed to reveal a tumor. The removal of a normal parathyroid gland produced no changes in the blood picture. A second exploration was equally unsuccessful, and even though the left lobe of the thyroid gland was removed, no parathyroid tissue was found. The tumor was finally found within the right thyroid lobe.

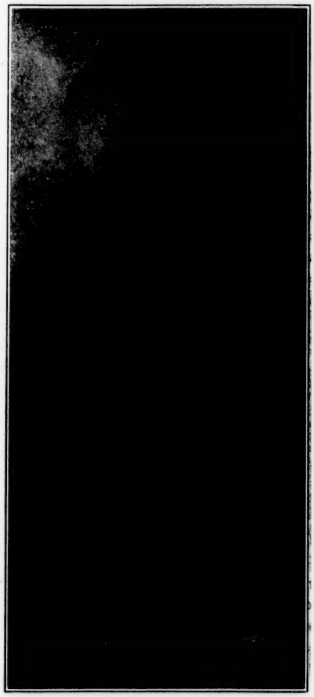

FIGURE 2. *Case 1.*
The x-ray film shows multiple cysts of the humerus, with almost complete absorption of the cortex.

Following the last operation the blood showed an immediate drop in calcium and phosphorus, with a later return of the phosphorus to normal but a persistently low calcium. Symptoms of tetany were controlled with large amounts of calcium and parathormone. The fatal termina-

tion as a result of kidney damage and infection was to be expected.

This case well illustrates the difficulty of finding parathyroid tumors, or even normal parathyroid glands. A persistently careful exploration of the neck at the first operation in the usual location of parathyroid glands, the retrotracheal and esophageal areas and the mediastinum proved fruitless. Only one of the two masses removed from the right side of the neck proved to be parathyroid tissue. Inasmuch as the tumor was subsequently found within the thyroid gland on this side, presumably all parathyroid tissue was removed from this side, yet no glands were

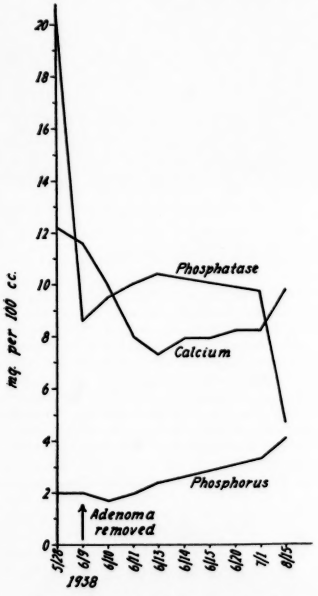

FIGURE 3. *Laboratory Data in Case 2.*

found in the left thyroid lobe removed at the second operation, and none were found on post-mortem examination. The question arises whether this patient had only two parathyroid glands, or whether both surgeon and pathologist were incapable of identifying them.

CASE 2. C. R. J. (B. C. H. 900326), a 39-year-old man, entered the hospital on May 26, 1938, because of rheumatic pain in both knees for 2 years, which was aggravated by climbing stairs. Six months before admission, his left knee became swollen and painful. This gradually subsided, but was followed by a swelling below the right knee.

Examination showed a hard, slightly tender mass about 8 cm. long and 4 cm. wide on the anterior surface of the right tibia in the upper third. There was no limitation of motion in the joint. Physical examination was otherwise negative.

Examination of the blood showed calcium 11.8 mg., phosphorus 2.0 mg., nonprotein nitrogen 20 mg., blood sugar 87 mg., cholesterol 128 mg. and phosphatase 20.6 (Bodansky) units per 100 cc. (Fig. 3). X-ray examination showed degenerative cystic changes of both tibias and patellas and of the pelvis, ribs and skull. A biopsy specimen from the right tibia showed osteitis fibrosa cystica, with osteoid formation in part and benign giant-cell tumor elsewhere.

On June 9, the neck was explored through the usual collar incision. The pretracheal muscles on the right were divided between clamps, and the right thyroid lobe freed and rotated toward the mid-line, exposing a tumor the size of a large olive on its posterior surface amid terminal branches of the inferior thyroid artery. It was yellowish brown. A portion was removed for diagnosis, and a frozen section showed a parathyroid adenoma.

About three fourths of the tumor was resected, and the wound closed without drainage. The portion removed weighed 5.5 gm., and the estimated weight of the tumor itself was 7.5 gm. Twenty-four hours after the operation the blood calcium had dropped to 10 mg., the phosphorus to 1.7 mg. and the phosphatase to 8.6 units per 100 cc. The calcium reached its low point of 7.3 mg. on the 3rd day. The phosphorus steadily rose until it was normal. The phosphatase remained elevated for some time.

The convalescence was uneventful, save that on the 4th postoperative day there were mildly positive Chvostek and Trousseau signs. These disappeared under treatment in 4 days.

On August 15, the blood calcium was 9.8 mg., the phosphorus 4.1 mg., and the phosphatase 4.7 units per 100 cc. Subsequent check-ups have shown the blood chemical findings to be normal. The patient is symptom free, and the bony defects have recalcified.

Comment. The blood chemical findings and bone picture in this patient were typical. The tumor was readily located, and its appearance was such that it could not be mistaken for any other tissue. The tumor was not entirely removed because I wished to avoid the severe symptoms of tetany encountered in Case 1, and believed that if necessary more could be easily removed later because of its accessibility. Fortunately, the amount resected proved sufficient.

CASE 3. F. K., a 68-year-old man who worked as a foundry foreman, entered the Faulkner Hospital on December 26, 1939, having been referred by Dr. Gerald L. Doherty. Three weeks before admission his right hip was injured by the premature closing of a street-car door. The hip was painful, but he managed to get about. He thought it to be rheumatism, and consulted an osteopath. Four treatments aggravated the pain. He was then seen by Dr. Doherty, who diagnosed the case as a fracture of the neck of the right femur, and sent him to the hospital. The diagnosis was confirmed by x-ray study, and the previous history was suggestive of a pathologic fracture. The patient was well until September, 1938, when he fell and fractured his right clavicle. This healed within a month. In January, 1939, he again fell and fractured the neck of his left humerus. This also healed promptly. In May he fractured the neck of his right humerus. All these fractures healed rapidly, and in none was an x-ray film taken.

His general health had been excellent, save for the fractures. He had lost 10 or 12 pounds in the year preceding entry.

The reflexes were normal. The heart was somewhat

enlarged to the left, but the sounds were of good quality. There were no murmurs. The lungs were clear save for rales at both bases. The liver edge was four finger-breadths below the costal margin and not tender. There was no edema. The prostate was small and nontender. There was a deformity of the outer third of the right clavicle, and also a deformity of the right hand in the 3rd metacarpophalangeal joint. The right leg was shorter than the left; the foot was everted, with an overriding of the shaft of the femur on the neck. The spine was normal. The blood pressure was 156/90.

Three days after admission extensive x-ray examinations showed: old fractures of the left 7th and 8th ribs posteriorly, and of both humeral surgical necks and both clavicles; a recent fracture of the neck of the right femur;

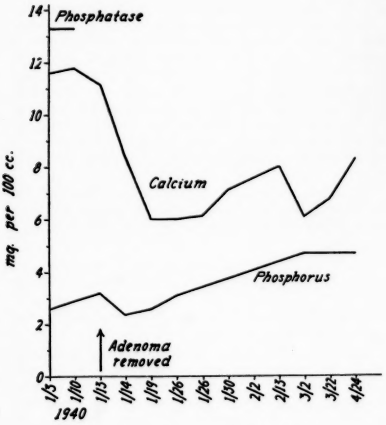

FIGURE 4. *Laboratory Data in Case 3.*

a questionable incomplete fracture of the neck of the left femur; slipping of the 5th lumbar vertebra forward on the sacrum with hypertrophic changes; cystlike cavities in lower ends of the femurs, with decalcifications; generalized osteoporosis, with coarseness of bone trabeculations suggestive of a metabolic disease; a question of stone in the right kidney; and cystic areas in shafts of both humeri, the upper end of the right radius and both tibias. A diagnosis of osteitis fibrosa cystica was made.

The blood calcium was 11.6 mg., the phosphorus 2.6 mg., and the phosphatase 13.3 (Bodansky) units (Fig. 4).

On January 9, 1940, x-ray study of the gastrointestinal tract was negative. X-ray films of the chest showed the transverse diameter of the heart to be 13 cm. The left ventricle was slightly prominent, and the aorta elongated and tortuous. In the right upper mediastinum, extending as low as the aortic arch, was an oval mass 4 by 6 cm. (Fig. 5). The trachea was displaced to the left by the mass, which lay on the right of and posterior to the trachea. The trachea was slightly narrowed at this point. The mass moved with the trachea on swallowing. The appearance was that of an intrathoracic goiter, but the question was raised as to its being a parathyroid tumor.

On January 13, the thyroid gland was exposed through the usual collar incision. The pretracheal muscles on the right were divided between clamps. Both superior and inferior thyroid arteries on the right side were ligated, and the right lobe was rotated medially. Continuous with the lower pole was an intrathoracic mass the size of a plum, which was easily delivered from the chest. The tumor was brownish and appeared to be an enlarged

FIGURE 5. *Case 3.*

This is a spot film of the mass on the right of the deviated and compressed trachea.

parathyroid gland that had migrated downward from its normal location near the lower pole of the thyroid gland to lie posterior to the trachea. The mass was excised, and a frozen section showed it to be a parathyroid adenoma. The mediastinum was drained and the wound closed. The pathological report was as follows: The specimen was an ovoid nodule 5 by 2.5 by 3 cm., weighing 25 gm. (Fig. 6), which by microscopic examination proved to be a parathyroid adenoma.

On the 6th postoperative day the blood calcium reached its lowest level, 6.0 mg. per 100 cc.; the phosphorus was 2.6 mg. It was probable that this level had been reached

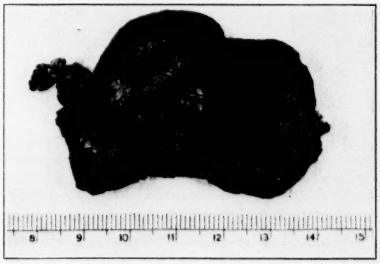

FIGURE 6. *Case 3.*

The tumor mass after surgical removal.

by the 3rd postoperative day, since at that time the patient became very irritable, nervous and apprehensive. On the 5th day, although Chvostek and Trousseau signs were absent, he developed a tremor and muscular twitchings. The positive signs developed in about a week. He de-

veloped bladder tetany, had to be catheterized and was eventually put on constant drainage. A high nonprotein nitrogen was improved by forcing fluids, and as soon as the chlorides were normal, the saline solution was changed to glucose. At this point, on the advice of Dr. Joseph Aub, the patient was given a much larger dose of calcium and parathormone, and from then on steadily improved. By the end of the 2nd week, he had been taken off constant drainage, was able to void, was sitting up in a chair and had recovered his usual cheerful disposition. The parathormone had been decreased, and he then was given dihydrotachysterol (A.T. 10).

He was discharged from the hospital February 8, much improved. Recalcification of his bones was beginning to be evident by x-ray films. Further x-ray study on May 10 showed still further recalcification. The dihydrotachysterol was discontinued in May, and in August the hip was solidly united and the patient was back at work.

Comment. This patient was considerably above the average age for this disease. It is remarkable that he could have sustained multiple fractures in a 2-year period without x-ray check-up, and without the suspicion that pathologic fracture might have arisen. The bone and blood picture was typical. The location of the tumor was uncertain, although the intrathoracic tumor suggested that a parathyroid gland had descended into the chest with the lower pole of the thyroid.

When the large parathyroid tumor was delivered, it was deemed best to remove it entirely, because its uncommon location would have made a secondary operation hazardous. Also the trachea was deviated and constricted, and it was necessary to remove this source of pressure.

The immediate drop in calcium and phosphorus was characteristic. The postoperative symptoms, as anticipated, were rather severe and prolonged, but eventually recovery was complete. The patient required a great deal of treatment, and his kidney function was much impaired in the early part of the postoperative course. This patient showed the shadow of a probable stone in the right kidney. Dihydrotachysterol was very useful and was continued for 4 months before his calcium balance was completely re-established.

Summary and Conclusion

Three proved cases of parathyroid adenoma together with their significant findings are reported.

In two cases, the tumor was found in an unusual location. Both patients had evidence of impaired renal function and kidney stones.

The uneventful convalescence and recovery of a patient with a large adenoma in a normal position suggests partial resection rather than complete removal as the operation of choice.

319 Longwood Avenue

Discussion

Dr. Edward D. Churchill, Boston: Dr. Cochrane has presented us with three museum pieces of parathyroid disease, scientifically studied and skillfully handled from the surgical point of view. There are so many aspects that might be discussed that I shall very rigidly confine myself to a few notations about the operative management.

The first problem in parathyroid surgery is to find the tumor. Dr. Cochrane and I were talking last night about the psychologic state of the surgeon toward the end of the second hour of a search for a parathyroid tumor, and the necessity at that time of having a positive diagnosis to stiffen his courage. A similar psychologic state is met when one faces the necessity of operating for the second, third or fourth time on a very sick patient. Hyperparathyroidism is a diagnosis that cannot be disproved by surgical dissection. Even if four normal parathyroid glands are found, there may be a fifth somewhere in a remote region of the mediastinum that cannot be reached.

A large mediastinal tumor may be demonstrated by esophageal deformity with a swallow of barium. Tumors of the posterior mediastinum are usually large and are apt to be anchored in the neck by an attachment in the region of the inferior thyroid artery. Those in the anterior mediastinum represent an embryologic descent or an origin from one of the lower branchial clefts. It is the anterior mediastinal tumor that is most likely to give the greatest surgical difficulty. If the tumor is large, it can be delivered as a substernal goiter is delivered, but there is no chance of reaching or palpating a tiny fragment of soft tissue that is low. The only answer to this problem is a manubrium-splitting incision that affords direct visual access to the anterior mediastinum. Here again one has to be backed up by a positive diagnosis.

Dr. Ernest M. Daland, Boston: I should like to call attention to an article in a recent number of the *British Journal of Surgery*. The writer noticed that in some cases of parathyroidism, both when the tumor had been removed and when it had not, there had not been proper regeneration of the bone around the cyst. He devised a scheme of using aluminum acetate in large quantities, given by mouth, and reports a large number of cases in which he has had prompt regeneration of the cysts in cases in which they had failed to regenerate following the customary therapy.

The mechanism apparently is such that the acetate salt combines with the phosphates, forming aluminum phosphate. This allows the calcium to be deposited. The author mentioned above has also used this in a number of cases of rheumatoid arthritis, which he considers to be a dysfunction of the parathyroid glands, with excellent results.

Dr. John Homans, Boston: Of course, the fascinating side of this technical procedure is the discovery not only of the tumor itself but also of the other parathyroid glands. A good deal of stress has been laid by Dr. Cochrane and Dr. Churchill on finding these tumors well inside the mediastinum. As a matter of fact, during the third hour of a search for one of these tumors, while I was hopefully opening the jaws of a hemostat here and there over the operative field, having looked behind the trachea and esophagus, I happened to insert and open my snap at the junction of the superior thyroid artery with the external carotid, and there at the apex — of course, the superior thyroid artery slants rather downward — was a good-sized parathyroid tumor.

The tendency is to look downward, whereas this time the tumor was in an unusually high position.

Dr. Cochrane (closing): What interested me in the first patient was that after I had presumably removed all the parathyroid glands on the right side, and had apparently missed the parathyroid glands when I took out the left lobe of the thyroid, the pathologist at post mortem could find no remaining parathyroid tissue. It raised the question whether the patient actually had four parathyroid glands or only two or three.

I want to emphasize again the point Dr. Churchill brought out about the psychologic handicap to the surgeon in the cases in which one has the typical bone picture but not the typical blood chemical findings. After one has searched for two hours unsuccessfully, in an atypical case, there is a doubt in one's mind whether to go on and subject the patient to any more search.

Dr. Lahey called me the day before yesterday to say he was sorry he could not come to discuss the paper. He told me that he had just operated on a patient who, he was absolutely convinced, had a parathyroid adenoma, but that he had failed to find the tumor. Previously three excellent surgeons had explored the neck without success. This emphasizes the fact that it is an extremely difficult thing to find the parathyroid glands, even when one is positive that a tumor is present.

STAPHYLOCOCCAL TRACHEOBRONCHITIS TREATED WITH SULFAMETHYLTHIAZOLE AND SULFATHIAZOLE

Report of Two Cases

MAURICE H. SHULMAN, M.D.

SALEM, MASSACHUSETTS

EACH of the recent developments in the field of chemotherapy has been followed by a flood of confusing reports and claims. Sulfamethylthiazole and sulfathiazole have been no exception. A survey of the literature shows consistently good results obtained in staphylococcal infections.

Bacteriologic experiments conducted by Rake and McKee[1] have shown sulfamethylthiazole and sulfathiazole to be particularly effective. This is further substantiated in a report by Krock and Chamberlain.[2]

Many different types of staphylococcal infections have been successfully treated with these drugs. Grulee and Mason[3] report excellent results in cases of furunculosis in children. Fitch[4] obtained noteworthy results in a case of epidural abscess with septicemia and pyemia due to *Staphylococcus aureus*. Another case of staphylococcal septicemia, with excellent end results following the use of sulfamethylthiazole, is reported by Carroll et al.[5]

In a study of the literature one is immediately aware of the many toxic effects of these drugs. Pepper and Horack[6] report the formation of concretions in the renal tubules following sulfathiazole therapy. Knoll and Cooper[7] also report clinical urolithiasis due to sulfathiazole. Haviland and Long[8] report conjunctival and scleral reactions in the course of such therapy. Further study of these reports reveals that the aged are more susceptible to these toxic effects than patients in the younger age groups.

The two cases reported in this communication throw light on the use of sulfamethylthiazole and sulfathiazole in staphylococcal laryngotracheobronchitis. The former was originally supplied by the Winthrop Chemical Company for experimental purposes only, but was then withdrawn from the market because of reports of toxic effects; the latter was used in the second case. The initial dosage of both drugs in these cases was 1½ gr. per pound of body weight, given in four doses. The daily dosage thereafter was 1 gr. per pound of body weight.

CASE REPORTS

CASE 1.* A 2-year-old girl was admitted to the Salem Hospital in February, 1940, after an illness of 3 days. She had had malaise and hoarseness, with some fever, at home. Hoarseness became progressively worse, and the patient developed cyanosis during a coughing spell. Breathing became more labored, and the patient was hospitalized.

The family history was noncontributory. The patient was the only living child. At 3 months of age she developed mild eczema, which was much less intense on admission. The developmental history was normal. The patient had received injections of Sauer's vaccine, but no other immunizations had been performed. The present illness was the first real illness that the patient had had.

On entry physical examination revealed an acutely ill girl, who was markedly apprehensive and restless. The lips and nailbeds had a grayish, cyanotic tinge. There was some inspiratory difficulty, with slight substernal retraction. The respirations were noisy and wheezy. The tonsils were reddened, but no membrane was present. Auscultation of the chest revealed harsh rhonchi and sibilant and sonorous rales at both bases. The remainder of the examination was negative.

A diagnosis of laryngotracheobronchitis was made, and the patient was seen by an otolaryngologist. Expectant treatment was immediately instituted. This consisted of a croup tent and careful use of Sodium Amytal for restlessness. Throat smears revealed gram-positive organisms, tentatively called pneumococci, and sulfapyridine by mouth was given. Early in the morning of the day following admission, the patient had a choking spell and became cyanotic; the respirations were shallow and labored. A Mosher lifesaver was passed, and an emergency tracheotomy was done. Throat culture taken at entry grew a pure culture of *Staphylococcus aureus* (hemolytic). Sulfamethylthiazole was started with a Levine tube. For the next 7 days, the patient had a stormy course. The tracheotomy tube frequently became plugged up by thick, yellowish

*Reported through the courtesy of Dr. Robert T. Moulton.

crusts. The temperature varied from 101 to 105°F. The respirations remained about 40.

For 5 successive days the patient had a positive blood culture for *Staph. aureus*. The blood level of the sulfamethylthiazole was kept between 3 and 5 mg. per 100 cc. On the 5th day of medication, a morbilliform rash appeared. This was considered to be a drug rash and subsided in a few days. Several blood transfusions were given. Sulfamethylthiazole was discontinued slowly. The urine showed a positive culture for *Staph. aureus* at one time, and frequently showed red blood cells and white blood cells in the sediment.

The tracheotomy tube was removed on the 17th day, after which the patient did very well. The wound healed rapidly, and the patient was discharged recovered on the 23rd day following admission.

Case 2. W. M., a 1-year-old boy, had been very well until June 22, 1940. At that time the patient was first seen at home, and a diagnosis of "croup" was made. He became progressively worse, and breathing was much more labored. Failing to respond to routine treatment, the patient was admitted to the Salem Board of Health Hospital.

The family history was not remarkable except for marked allergy. One brother, 4 years old, had had severe eczema. The feeding history was uncomplicated except for slight eczema, which cleared up when the patient was put on an evaporated-milk formula. The developmental history was normal. The patient had received Sauer's vaccine and diphtheria toxoid.

At home the patient had a temperature of 100°F. by rectum, and respirations up to 40 per minute. No cyanosis was noted until entry on June 24. He was quite restless. At the onset of the disease, the patient had some inspiratory difficulty and no substernal retraction. Inspiration became more difficult, and the substernal retraction very marked. The chest was clear to auscultation. The throat and tonsils were red. The remainder of the physical examination was negative.

On entry to the hospital, a diagnosis of laryngotracheobronchitis was made. Because of progressive difficulty in breathing, in addition to the appearance of cyanosis, an otolaryngologist saw the patient immediately on arrival at the hospital. Tracheotomy was done at once. When the larynx was opened, the patient coughed up several large plugs of pus and immediately fell asleep. Culture of these plugs grew a pure culture of *Staph. aureus*, which was slightly hemolytic.

A tracheotomy tube was secured in situ, and the patient was placed in a steam-filled room. As soon as reports of the throat cultures were obtained, he was started on sulfathiazole. Repeated blood cultures were negative. Several cultures taken from the tube grew *Staph. aureus* with hemolysis in pure culture.

For 4 days after tracheotomy was done, the temperature remained about 103°F., the pulse 150, and the respirations about 40. The course was quite stormy, and several times the tracheotomy tube became obstructed by thick plugs of mucus.

On the 5th day, the urine sulfathiazole had reached a level of 30 mg. per 100 cc., and the temperature and respirations became normal. The pulse remained about 120. Convalescence was much smoother after the 5th day, but plugs of mucus collecting in the tracheotomy tube continued to be very troublesome and required constant watching.

Sulfathiazole was gradually withdrawn and finally omitted on July 7, after 14 days of administration. The temperature, pulse and respiration did not rise above normal. The hemoglobin never fell below 60 per cent, and the red-cell count was never below 3,340,000. With administration of iron by mouth, the hemoglobin was 80 per cent and the red-cell count 4,000,000 on discharge.

On July 8, 15 days after insertion, the tracheotomy tube was removed, with no ill effects. The wound healed rapidly, and the patient was discharged recovered on July 14, exactly 3 weeks after tracheotomy was done.

Summary and Conclusion

The literature on sulfamethylthiazole and sulfathiazole is reviewed. Special emphasis is placed on the toxicity of these two drugs, the former having been withdrawn from the market by the manufacturer.

Two cases of staphylococcal tracheobronchitis necessitating tracheotomy are reported. The first case was associated with a staphylococcal bacteremia, hitherto nearly 100 per cent fatal. In both, staphylococci were recovered in pure culture from the throat or coughed-up plugs.

The value of sulfamethylthiazole and sulfathiazole in combating staphylococcal infections is substantiated by the successful outcome of these two cases.

60 Washington Square

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MEDICAL PROGRESS

PLASMA PROTEINS IN HEALTH AND DISEASE*

ROBERT F. LOEB, M.D.†

NEW YORK CITY

ONE hundred and fourteen years ago, Dr. John Bostock,[1] chemist and physiologist of Guy's Hospital, studied urine and blood from Richard Bright's dropsical patients. In addition to his classic observations on the characteristics of the urine, Bostock reported to Bright, "I think I may venture to say, that the serum generally in these cases contained less albumin than in health, although I am not able to state precisely the amount of this difference." Thus, in 1827, a disturbance in the normal pattern of the serum proteins was established as a chemical characteristic of a diseased state.

In the field of immunology, von Behring[2] demonstrated in 1890 that the injection of attenuated diphtheria toxin into animals resulted in the formation of antitoxin in the serum, which could be employed for preventive or therapeutic inoculations. Since these immune substances are now known to be modified serum globulins, the practical as well as the theoretical importance of the serum proteins in the field of immunochemistry becomes obvious.

In 1896, Starling's[3] simple and yet decisive observations on the relation between the hydrostatic pressure in the capillaries and the osmotic pressure of the serum proteins gave rise to a now familiar physiologic concept of extraordinary importance. Although Starling's work is well known, I cannot resist quoting some of the conclusions drawn by him on the basis of his experiments. He measured the return of fluid to the blood stream following the perfusion of edematous limbs, and correlated the relation of the hydrostatic pressure in the capillaries with the effective osmotic pressure of the serum proteins, which he measured directly. Starling wrote:

> At any given time there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood in the capillaries for the surrounding fluids. With increased capillary pressure there must be increased transudation — with diminished capillary pressure there will be an osmotic absorption of salt solution from the extra vascular fluid. . . .

The significance of these representative contributions from the field of clinical medicine, immunology and physiology is apparent. Nevertheless, Morawitz,[4] who himself developed in 1906 the technic now termed "plasmapheresis" for the study of the regeneration of serum proteins, wrote in 1909, "Many studies of blood serum in various disease conditions are on record . . . but little of importance to pathology and physiology has been gained." Our ignorance of many elementary facts concerning the serum proteins even today is great, yet this need not be a cause for discouragement. Few problems have sustained the interest and engaged the investigative activities of physicists, chemists, immunologists, physiologists and clinicians more than those concerning the serum and plasma proteins. The progress made in recent years concerning the nature of the plasma proteins, their source, their regeneration, their abnormalities in various diseased states, the physiologic disturbances attendant on their depletion, as well as their therapeutic value in the correction of certain physiologic disorders, is truly gratifying. It is toward certain aspects of this progress that I desire to draw attention in this review.

STUDY OF THE NATURE OF PLASMA PROTEINS

One of the ultimate aims of the chemist is to identify beyond question the nature of a substance by means of establishing its structure. In the field of protein chemistry, this aim is yet to be attained. This is true even though the percentages of various amino acids present in many proteins are well established and many of the linkages of amino acids and peptides have been recognized through the work of Bergmann[5] and others in the last fifteen years. Thus, although insight into the complex structure of the protein molecule has been gained by means of these studies of the action of various enzymes on synthetic and known substrates, the groupings that lead to the specific characteristics of proteins remain obscure. The difficulties in solving the problems of the chemistry of the proteins center about the enormous com-

*From the Department of Medicine and the Department of Neurology, College of Physicians and Surgeons, Columbia University, New York City.
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†Professor of medicine, College of Physicians and Surgeons, Columbia University; associate attending physician, Presbyterian Hospital.

plexity of the molecules, many of which include side chains of lipids and carbohydrates. Moreover, many of the proteins undergo denaturation with even the gentlest chemical manipulation.

The chemistry of the plasma and serum proteins naturally constitutes only a special problem in general protein chemistry. In default of essential knowledge, serum proteins are today, as in the past, classified on the basis of convention. Thus the protein of the plasma or serum that remains in solution after half saturation with ammonium sulfate or is not precipitated by 21.5 per cent sodium sulfate is defined as albumin. The proteins salted out by these means are known as globulins. By using lower concentrations of salt solutions for precipitation, the globulins are subdivided into fractions termed euglobulin, pseudoglobulins I and II and fibrinogen. Salting out continues to be the accepted method for determining the presence and concentrations of various serum protein fractions. This procedure yields information that has been of immeasurable value in the practical preparation of immune serums, in the characterization of a number of diseased states to be discussed, and in the vast majority of studies devoted to the physiologic importance of the serum proteins. Nevertheless, it must be recognized that the fractions thus estimated embrace a large number of proteins with strikingly different characteristics, and that the various components often represent loose chemical combinations of two or more proteins. The true albumins have been shown repeatedly to have a molecular weight of the order of 70,000 and those of the globulins approximately 170,000.

In the last decade, three new approaches have been applied to the study of the serum proteins. These include: first, the technic of ultracentrifugation; secondly, electrophoresis; and thirdly, the application of immunochemical reactions.

The ultracentrifugation method developed by Svedberg[6] for the study of protein solutions consists in sedimenting the molecules from a solution by means of centrifuges of special construction. These centrifuges are capable of developing rates up to 200,000 revolutions per minute, and are fitted with optical contrivances making it possible to record photographically by means of various lengths of visible and ultraviolet light the rate of sedimentation of various solutes. In this way the molecular weights of one or more substances can be determined, since the rate of sedimentation is a function of the mass of the molecule and the centrifugal force. This method also offers a valuable check on the purity of a given solute, — in this review, a serum protein, — since the substances of different molecular weights will be sedimented at different rates and different stratums of molecules appear in the photographs obtained.

The second technic, which is proving of great value both chemically and clinically in the study of serum proteins, is in reality an old one. In 1899, Hardy[7] demonstrated the migration of colloidal particles in an electric field. This phenomenon is termed "electrophoresis." The method was later successfully employed by Michaelis[8] to distinguish certain enzymes and proteins by their mobilities and their isoelectric points. This electrophoretic technic, which is in principle identical with that of measuring the mobility of ordinary ions, has been modified in recent years. Tiselius[9] has made it possible to record accurately the rate of migration of various proteins, and to separate these fractions for subsequent analysis by other means without altering their chemical nature by polarizing or heating currents. These measurements are made under standard conditions of pH, ionic strength and temperature. Like the ultracentrifuge, the boundary of the migrating molecules can be recorded photographically, employing what is known as the Toepler-Schlieren method. This depends in principle on the detection of "small inhomogeneities in refractive index," caused in the serum proteins by the boundaries of the various protein fractions, migrating at different velocities. Longsworth et al.[10, 11] have ingeniously modified further the method of Tiselius and of Philpot[12] for recording the velocity of migration of various solutes. From the curves obtained by his method, calculation of the concentration of various solutes is made possible, in addition to separation of these on the basis of their velocity of migration. In Figure 1 may be seen curves obtained by Longsworth et al.

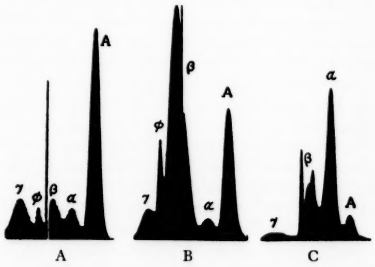

FIGURE 1. *Plasma and Serum Protein Analyses Derived by the Electrophoretic Method (after Longsworth, Shedlovsky and MacInnes[10]). (Reproduced by courtesy of the publisher.)*

A = *normal plasma;* B = *plasma from a case of multiple myeloma;* C = *serum from a case of nephrosis.*

in the electrophoretic analysis of normal human plasma, the plasma from a patient with multiple myeloma and the serum from a patient with nephrosis. In curves of this type, the area of a peak is a function of the concentration of a fraction of a definite migration velocity. The homogeneity of a fraction is determined by the slopes of each peak. For example a peak with a narrow base suggests that one or more substances of essentially the same mobility are present. A broad peak speaks for the probable existence of substances of varying mobilities, which probably represent mixtures.

The analytical results obtained for the total albumin and globulin fractions of normal human serums by electrophoresis and the conventional salting-out method are generally in good agreement. It must be pointed out, however, that the alpha, beta and gamma fractions of the globulin, as separated by the electrophoretic method and as named by Tiselius, do not correspond to euglobulin and pseudoglobulin as measured by salt precipitation.

In abnormal serums, marked discrepancies may appear between the analytical results obtained by the two methods. Certain fractions with the mobilities of the globulin may be erroneously found in the albumin fraction as determined by the usual technic, and the globulin abnormalities as determined by both methods show but little agreement.

In the last thirteen years the brilliant studies of Heidelberger[13] and his associates have contributed significantly to the view that antigens and antibodies are proteins of specific chemical nature. Heidelberger has furthermore established beyond reasonable doubt the fact that antigen and antibody combine, under controlled circumstances, in accordance with the laws of multiple proportions, which govern more familiar chemical reactions.

Kendall,[14] who participated in these studies, has utilized the basic knowledge obtained for the immunochemical analysis of human serum protein by precipitin reactions. Beginning with the immunization of rabbits with water-soluble and water-insoluble euglobulin and pseudoglobulin from the salted-out protein of normal human serums, Kendall prepared antiserums. It developed from a quantitative study of precipitates formed by these antiserums and solutions of the salted-out protein fractions that there are three globulin fractions. This was also found to be true with the electrophoretic method. The quantitative correlation between the precipitin method of Kendall and the usual salting-out method as applied to the total amounts of albumin and globulin in normal serums is excellent. In certain diseased states, the immunochemical technic applied by Goettsch and Kendall,[15] like that of the Tiselius electrophoretic method, indicates that qualitative as well as quantitative changes occur in the various serum protein fractions. Thus, Goettsch and Lyttle[16] have shown that abnormal albumins and globulins appear in the serums of nephrotic patients. These proteins do not react to form precipitates with the antiserums prepared from normal serum albumin and globulin. Furthermore, antiserums prepared from the abnormal serum proteins obtained from nephrotic patients do not react with normal serum albumins and globulins. As much as 25 per cent of the serum albumin and globulin in a nephrotic patient may differ in its chemical nature from the protein normally present. These qualitative differences cannot be detected with the usual salting-out method.

It is hoped that this fragmentary review may serve to indicate the various means that are today being employed to advance the knowledge of the chemical characteristics of the serum proteins. These procedures for the main part measure different properties of the proteins. It is to be anticipated that the integration of the results obtained from the simultaneous application of these methods may continue to advance knowledge in this complex field of chemistry.

Origin of Plasma Proteins

The origin of the plasma proteins has always been an intriguing problem. There is at the present time no direct proof of the source of any of them. There continues to accumulate, however, indirect evidence, which carries at least a measure of conviction particularly concerning the origin of two, namely, fibrinogen and prothrombin. These two proteins of the plasma show, with considerable regularity, a striking decrease with destruction of liver tissue, and their decrease more or less parallels the degree of liver damage present. As a matter of fact, the concentration of circulating fibrinogen was at one time used as a test for hepatic function. More recently, various workers have suggested that the lack of prothrombin regeneration following the parenteral administration of vitamin K in patients with parenchymatous liver degeneration be employed to appraise liver function. This test has also been recommended to distinguish between the icterus of obstructive and that of degenerative origin, because in obstructive jaundice prothrombin plasma levels rise promptly following vitamin K administration. Added to this evidence is the significant fact that damage to other organs does not result in a decrease in fibrinogen and prothrombin, provided the liver remains intact.

Concerning the source of the other plasma proteins, Madden and Whipple[17] have recently stated,

"One who is acquainted with the literature hesitates to bring up the subject of the *origin of albumin and globulin*." It is, however, the conviction of Madden and Whipple that "evidence speaks in favor of the liver as the site of production of albumin and of much of the globulin."

The evidence that favors the liver as the site of serum albumin formation is suggestive but at the same time not wholly convincing. It is based on the following facts. First, that Eck-fistula dogs, as first shown by Kerr, Hurwitz and Whipple,[18] are apparently able to regenerate only about one tenth as much plasma protein as normal dogs and that these dogs are known to undergo liver atrophy. Secondly, Elman and Heifetz[19] have shown a marked decrease in liver function, as tested by isoiodeikon excretion, in dogs developing hypoalbuminemia on Weech's[20] protein-deficient diet. These dogs also show vacuolization of the liver cells, a condition which accompanies a decrease in the level of serum albumin. This decrease in serum albumin has recently been shown by Patek and Post[21] to be associated with an inability of certain patients with cirrhosis to form serum albumin even when large amounts of protein are fed. That proteins other than plasma proteins are stored by these patients is shown by their marked positive nitrogen balance. The presence of marked hypoalbuminemia, as defined by a level below 2.5 gm. per 100 cc., which persists despite an adequate protein intake, constitutes a grave prognostic sign in cirrhosis and suggests the presence of irreparable liver damage.

Hypoalbuminemia in the nephrotic state and the classic failure of this hypoalbuminemia to respond to high-protein feeding throws some doubt on the specificity of the liver as a source of serum albumin, because at the present time there is little evidence to suggest that either functional or anatomic liver damage exists in nephrotic patients. It may be argued that long-continued albuminuria exhausts the capacity of the liver to regenerate serum albumin in these patients. On the other hand, when the serum albumin has been decreased for only a short time, it is also often impossible to raise the albumin level despite a positive nitrogen balance maintained over the course of many months. This reasoning does not in any way exclude the liver as the source of serum albumin, but it does raise an unexplained objection to the hypothesis.

With regard to the source of the plasma globulins, it is fair to state that most workers agree to a multiple origin. The importance of the liver in relation to fibrinogen and prothrombin formation is clear. In relation to the source of the other globulins, there appears to be less certainty about the role of the liver. Thus, there is an amazing lack of correlation between the changes occurring in the concentration of albumin and those occurring in the globulins in undernutrition. In Weech's[20] dogs maintained on an inadequate protein diet, as well as in human subjects, "the average concentration of globulin remains singularly constant; it follows that the fall in total protein is brought about entirely by depletion of the albumin fraction." The argument has already been advanced that the depletion of serum albumin in liver disease constitutes evidence that this type of protein is formed in this organ. At the same time, certain globulins of the serum are often strikingly increased in the blood in liver disease involving parenchymal cells, and yet it is suggested that much of the globulin is also formed in the liver. This apparent paradox might perhaps be explained if albumin and globulin are formed by different cells, for example, the albumin by polygonal cells and the globulins by the reticuloendothelial cells.

In the last two years Sabin[22] has provided convincing visual evidence indicating that the reticuloendothelial system as a whole is concerned with the elaboration of antibodies, which, as Heidelberger has shown by quantitative precipitin studies, may constitute as much as 60 to 70 per cent of all the serum globulins in highly immunized animals. Sabin injected a colored egg-albumin antigen prepared by Heidelberger into rabbits, and found that it was taken up by the cells of the reticuloendothelial system. The antigen was then altered by these cells by removal of the dye, and at this time it probably passed from vacuoles into the cytoplasm. After four to seven days, at which time antibodies appeared in the serum, the macrophages that had taken up the dye showed marked shedding of their surface films without damage to them. With the shedding of the surface films, Sabin believes that the antibody globulin is carried into the blood plasma. Sabin also believes that this shedding of globulin by cells of the reticuloendothelial system takes place at a slower rate in nonimmune animals, and that this process is responsible for normal serum globulin formation.

From this brief review of the origin of the plasma proteins, it is apparent that some light is being thrown on what continues to be a most confusing problem.

Regeneration of Plasma Proteins

I shall next consider plasma protein regeneration, a subject of considerable clinical as well as physiologic significance. Plasma protein depletion can be prevented in a number of ways in the normal animal. These may be enumerated as follows: the maintenance of an adequate dietary protein

intake; the maintenance of nitrogen equilibrium in the fasting animal by the intravenous administration of plasma proteins; the feeding of amino-acid mixtures in amounts sufficient to maintain nitrogen balance, in which the recent work of Mitchell and his colleagues[23] demonstrates that only seven of these acids are essential in the adult rat; the intravenous, subcutaneous or oral administration of casein hydrolysates to which are added tryptophan and cystine or methionine.

In the course of plasma protein depletion, as brought about in animals either by protein starvation, the technic employed by Weech, or by plasmapheresis in dogs maintained on a low but adequate protein intake, the method used by Whipple and his associates[17] for many years, the albumin fraction suffers primarily. This is particularly unfortunate for physiologic reasons. If protein depletion has been of short duration, repletion is rapidly accomplished by the means of protein feeding. If depletion is of long standing, the rate of protein repletion, as shown by Weech, is at first rapid, but then the pace is slowed and months may be required to attain the original levels. This is true not only in animals but also in man. Of interest, but still unexplained, is the fact that after depletion of certain reserve stores of plasma protein, the protein-starved animal is unable to utilize effectively his remaining body protein or its disintegration products for plasma protein regeneration.

In contrast to clinical states of hypoproteinemia brought about by undernutrition and curable by the methods that have been shown to prevent hypoproteinemia, stand cases of nephrotic and hepatic hypoalbuminemia. Regeneration of plasma proteins in these cases is notably ineffective, owing to a failure of the albumin-synthesizing mechanism. Treatment with high-protein diets or protein autolysates brings about the storage of body protein without regeneration of plasma protein, particularly serum albumin.

In recent years Madden and Whipple and also Weech have shown beyond question that the type of protein fed is of considerable significance in relation to its efficacy in bringing about plasma protein regeneration — this applies with certainty to albumin, which is of prime importance. Thus, it has been shown that beef serum protein has an extraordinarily high potency value in plasma protein regeneration. Beef muscle, casein, egg white and others are of medium potency, and of low potency are gelatin, zein, dog red blood cells and so forth, as shown in Table 1. Evidence concerning globulin regeneration is still controversial and fortunately of more purely academic interest.

In summary, then, plasma protein regeneration in hypoproteinemic states resulting from undernutrition can be corrected by the liberal administration of protein, amino acids or protein autolysates. Furthermore, in addition to the quantity of protein, its quality has been shown to be a matter of considerable importance. Finally, in states in which hypoproteinemia appears to be associated, at least in part, with a disturbance in serum albumin synthesis, administration of protein may lead to storage of body protein, with little if any increase in the serum protein concentrations.

TABLE 1. *Potency of Various Foods for Plasma Protein Formation.**

High Potency	Medium Potency	Low Potency
Beef serum	Egg white	Gelatin
	Autoclaved yeast	Zein
	Beef chuck	Pancreas
	Beef liver	Canned Salmon
	Casein	Red blood cells of dog
	Lactalbumin	Spleen
	Cooked pork kidneys	Beef stomach
	Polished rice	Pork brain

*Modified from Madden and Whipple.[17]

Disturbances of Serum Albumins and Serum Globulins in Diseased States

Modern medicine owes to a New York clinician, Dr. Albert Epstein,[24, 25] a great debt. His studies made between the years 1912 and 1917 on the disturbances of the serum proteins in disease and his application of the Starling hypothesis in the explanation of nephrotic edema served as a great stimulus for the mass of clinical investigation in this field in the past twenty-five years.

In the normal adult, the concentration of the serum proteins varies between 6 and 8 gm. per 100 cc. The proteins determined in the albumin fraction vary between 4 and 5.5 gm., and the globulins fluctuate between 1.5 and 2.5 gm. as measured by the three methods previously discussed. It has been customary in the past to lay great emphasis on the ratio of albumin to globulin. This tradition finds its origin in the work of Epstein. He pointed out in 1912 that the decrease in serum proteins in the nephrotic state did not result from hemodilution because, if this were so, the albumin globulin ratio would remain constant. In reality, the albumin fraction was found to be sharply decreased, and the globulin perhaps slightly increased. Thus, a change in distribution of albumin and globulin was established. Since the physiologic and clinical consequences of disturbances in the serum proteins depend on the actual concentrations of the albumin and globulin fractions, I urge that emphasis be placed on these rather than on their ratio. This can be explained as follows. An albumin globulin ratio of 0.5 is obtained when the albumin is 1.5 gm. and the

globulin is 3 gm. The same ratio is present when the albumin is 3 gm. and the globulin is 6 gm. It is obvious that the decrease in albumin is the striking feature in the first instance, and that an extraordinary increase in globulin results in the same ratio in the second instance. Certainly the physiologic, diagnostic and clinical implications are totally different despite identical ratios.

From the standpoint of the clinician, patients with disturbances in serum proteins may be separated into two categories: those in whom hypoalbuminemia and its consequences dominate the disease picture, and those in whom hyperglobulinemia is the outstanding abnormality. To this generalization may be added a corollary. Thus, abnormalities in the albumin fraction always occur in the direction of a decrease, whereas significant changes in the globulin fraction are associated with increases in these proteins. Albumin values greater than 5.5 gm. indicate either that dehydration or an abnormally soluble globulin is present. The presence of an abnormal globulin under these circumstances can be verified if the results obtained by the salting-out method,[26, 27] are compared with those obtained by the Tiselius or immunochemical technics of analysis. Although there is a sound physiologic and chemical basis for segregation of patients into these categories of hypoalbuminemia and hyperglobulinemia, it must be recognized that an outstanding disturbance in one protein fraction is often accompanied by some change in the other. For example, the serum albumin in a patient with cirrhosis of the liver may be reduced to 2.5 gm. per 100 cc., and at the same time the globulins may be increased to 5 gm. Or, in a patient with lymphogranuloma inguinale, as shown by Gutman et al.,[28, 29] the characteristic hyperglobulinemia is often associated with some degree of hypoalbuminemia.

The causes for hypoalbuminemia can be divided into three general groups: inadequate protein intake, excessive protein loss and failure of albumin regeneration. These groups of disturbances with their subdivisions are shown in Table 2.

Since the clinical importance of disturbances in serum albumin is dependent on its normal functions, these should be reviewed briefly. The serum albumin normally acts to maintain the effective osmotic pressure of the blood plasma, to maintain normal plasma volume, to serve as a source of energy in starvation, and to serve as a chemical buffer. The most important physiologic and clinical consequences of hypoalbuminemia depend primarily on a disturbance of one of these normal functions, namely, that of maintaining osmotic pressure. This activity follows from the fact that the albumin molecules traverse the capillary walls only in small amounts under normal conditions. Although this lack of permeability is also characteristic of the globulins, they exert but one fifth of the osmotic pressure of the albumin fraction in normal serum. The greater osmotic activity of the albumins results from their smaller molecular weight and their higher concentration in the serum. The difference in osmotic activity of the albumins and globulins in the blood is further accentuated by virtue of differences in their isoelectric points. These differences favor greater ionization and therefore greater osmotic properties of albumin at the pH of the blood.

TABLE 2. *Factors Causing Hypoalbuminemia.*

INADEQUATE PROTEIN INTAKE
Economic causes ("hunger edema")
Poor appetite
Any protracted illness
Cardiac decompensation
Chronic alcoholism
Mechanical interference with food intake
Poor intestinal absorption (?)
EXCESSIVE PROTEIN LOSS
Recurrent hemorrhage
Massive chronic suppuration
Exudation of serum (severe burns)
Uncontrolled diabetes mellitus
Nephrotic state
Various enteroenterostomies
Repeated abdominal taps
FAILURE OF ALBUMIN SYNTHESIS
Chronic parenchymatous liver disease
Nephrotic state
Cardiac edema with chronic passive congestion
Prolonged protein starvation (?)

Decreasing concentrations of albumin lead to a diminishing tendency for interstitial fluid to be brought back into the capillaries. In hypoalbuminemia, when the osmotic activity of the serum proteins at the venous end of the capillaries is less than the hydrostatic pressure, edema fluid will accumulate. This idea is in accord with the Starling hypothesis, the validity of which was established by the direct measurements of Landis.[30] Various workers have found that edema fluid tends to accumulate when the serum albumin concentration falls below a so-called "critical level." Thus, Moore and Van Slyke[31] observed that edema was usually present in patients in whom the serum albumin concentration was less than 2.5 gm. per 100 cc. In malnutrition, Bruckman and Peters[32] state that edema almost always develops when the albumin falls below 3 gm. per 100 cc. It is essential, however, to emphasize that other factors, such as the intake of sodium salts, the local renal factors of blood flow, glomerular filtration pressure, tubular reabsorption and tissue pressure, as well as unknown factors, may be of considerable importance. Thus, the rigid restriction of sodium salts tends to limit edema formation even in the presence of very low serum albumin concentrations. Also, striking diuresis may at times occur for

wholly unexplained reasons when the concentration of serum albumin is maintained well below the critical level.

From the foregoing discussion, it is apparent that marked hypoalbuminemia is characterized clinically by the physiologic tendencies that it may initiate. This is not true of hyperglobulinemia, the causes of which are presented in Table 3. The

TABLE 3. *Diseases Associated with Hyperglobulinemia.*

INFECTIONS	
	Lymphogranuloma venereum*
	Boeck's sarcoid*
	Lupus erythematosus disseminata*
	Periarteritis nodosa
	Subacute bacterial endocarditis
	Rheumatoid arthritis
	Leprosy
	Kala azar*
	Many other infections
NEOPLASMS	
	Multiple myeloma*
	Lymphoblastoma
	Leukemia
METABOLIC DISORDERS	
	Cirrhosis of liver*
	Cardiac failure (chronic passive congestion)
NO RECOGNIZED DISEASE	
	Occasional young Negroes

*Hyperglobulinemia often marked, that is, over 4.5 gm. per 100 cc.

heterogeneous groups of diseases in which increases in the globulin fraction of the serum occur include infections, tumors and metabolic disease. Hyperglobulinemia is also present at times in young Negroes who are otherwise apparently normal. No common underlying mechanism or mechanisms are as yet recognizable in these groups, although increases in serum globulins are often encountered in diseases in which plasma-cell reactions are prominent. The importance of hyperglobulinemia is, perforce, at the present time limited to its diagnostic value. This statement is not designed to detract from the clinical value of serum globulin determinations as an aid to diagnosis, but merely emphasizes the unsatisfactory state of knowledge concerning the physiologic interpretation of changes in the globulins. It is apparent from Table 3 that marked hyperglobulinemia, that is, values of more than 4.5 gm., occurs in but a limited number of diseased states and should therefore direct attention toward them. When hyperglobulinemia is of only moderate intensity, that is between 3.0 and 4.5 gm., the specificity of the disturbance is obviously reduced, and mild degrees of hyperglobulinemia are observed in an extraordinary variety of infections.

In addition to the diagnostic value of total globulin determinations, Gutman[33] has recently pointed out the usefulness of fractionation of the globulins. When the total concentration of globulin is increased, the euglobulin participates in the change with great regularity. In multiple myeloma, however, the euglobulin may not exceed its normal concentration of 0.1 to 0.2 gm. per 100 cc. Thus when a moderate or marked increase in total globulin is present and the euglobulin is not increased, Gutman has shown that the diagnosis of myeloma, which is often exceedingly difficult in the early stages, becomes relatively certain.

USES OF PLASMA PROTEINS IN THERAPY

It seems appropriate to end a survey devoted to the plasma proteins with a consideration of their role in therapy. Plasma protein or serum protein transfusions are recommended today in the treatment of two disorders, namely, hypoalbuminemia and the state of shock. These protein transfusions are employed instead of whole blood because they may, at least theoretically, have a greater effect in restoring the plasma protein levels to normal, in increasing and maintaining an increase in the circulating plasma volume, in initiating diuresis in hypoalbuminemic states associated with edema by virtue of raising the osmotic activity of the plasma and thereby increasing the plasma volume, and in making available a utilizable source of energy in states of undernutrition.

In the hypoalbuminemic state dependent on inadequate protein intake, the therapeutic implication appears to be an increase in the dietary protein. When this aim cannot be achieved, the daily infusion of casein autolysates should be the next therapeutic method of choice. When these methods fail, it is probably justifiable to employ plasma or serum transfusions, but it should be emphasized from the economic standpoint that, in this type of case, plasma transfusions constitute a true luxury. The same recommendations apply to the treatment of hypoalbuminemic states due to excessive protein loss. One notable exception must, however, be made. Thus in severe burns when shock is largely dependent on acute plasma loss, plasma or serum transfusion becomes the emergency procedure of choice.

It is in patients whose hypoalbuminemia is associated with the nephrotic state that plasma or serum transfusions are most frequently recommended. The hope in plasma or serum transfusions probably arises from the sound logic of the procedure in a group of patients in whom high-protein diets and casein autolysate infusions have been notoriously ineffective in stimulating serum albumin regeneration. Dramatic diuretic results have been reported by Aldrich and his associates[34, 35] in the treatment of nephrotic edema with lyophil serum. The experience of others has been less successful and suggests that the di-

uretic effects obtained were to be associated more with nonspecific reactions than with the concentrated plasma itself. My experience with plasma transfusions in nephrotic patients at the Presbyterian Hospital has been limited and truly disappointing. The following brief report is representative. A nephrotic boy, whose serum albumin was 1.3 gm. per 100 cc. before treatment, was given 2000 cc. of normal human plasma in the course of three days. It might have been anticipated that this amount of plasma would raise his serum albumin to at least 3.5 gm. In reality the serum albumin after three days was only 1.5 gm., and no diuresis occurred. The albumin transfused was either excreted in the urine or utilized as food, but it had none of the desired effects. Thus plasma transfusion in the nephrotic state is not so successful as has been hoped, but is well worth further trial, particularly if given in two to four times its normal concentration.

In the treatment of shock, the value of plasma and serum proteins has been demonstrated beyond question. There continues to be uncertainty concerning details of the best means of preparation, the optimal concentration for use and the relative values of plasma and serum. The fact that some disagreement and confusion exist concerning these details should in no way detract from the fundamental value of this type of therapy.

* * *

An attempt has been made to indicate the direction in which progress in knowledge of the problems of the serum proteins is being made. It is both interesting and significant that advances in understanding the physiologic aspects of these problems have developed simultaneously with the acquisition of empirical knowledge, which has, nevertheless, already been shown to have an important application in the practice of medicine. Thus knowledge of the mechanisms and diagnosis of disease has been enhanced materially.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 27231

PRESENTATION OF CASE

First Admission. A sixty-year-old woman entered the hospital for study.

Approximately one year before admission, the patient was treated in this hospital for erysipelas of the face, and during the routine examination a slightly tender, hard, irregular mass was palpated in the mid-epigastrium; it did not move with respiration. A gastrointestinal series revealed no evidence of intrinsic disease in the esophagus, stomach or duodenum. An extrinsic pressure defect on the medial side of the stomach corresponded to the mass felt through the abdominal wall. This mass was believed to be the left lobe of the liver, although the organ as a whole was not enlarged; the spleen was small.

Second Admission. A year passed before the patient again entered the hospital for an investigation of the mass. She had lost 6 pounds during the preceding few months, but even leading questions failed to uncover any subjective symptom.

On examination the patient was well developed and well nourished. The heart and lungs were normal, the blood pressure 160 systolic, 80 diastolic. The abdomen was soft, and an orange-sized, hard, nontender mass was palpable in the umbilical region, with its lower border on a level with the umbilical line. It was freely movable and moved with respiration. The right kidney was palpable; the liver was not.

The temperature, pulse and respirations were normal.

Examinations of the urine, stools and blood were negative. The nonprotein nitrogen of the blood serum was 20 mg. and the proteins 6.5 gm. per 100 cc.; the blood Hinton reaction was negative.

A gastrointestinal series showed a normal esophagus. The stomach was elongated and low in position but showed no defects, and the duodenal cap and loop were not remarkable. The palpable mass lay medial and posterior to the upper stomach, producing a pressure defect on the posterior wall at the junction of the upper and middle thirds. There were many small gallstones and one larger stone, apparently in the cystic duct.

A barium enema passed readily to the cecum and entered the terminal ileum. The colon showed a few diverticula in the region of the sigmoid, but otherwise was not remarkable. The palpable mass lay above and medial to the splenic flexure.

An operation was performed on the third hospital day.

DIFFERENTIAL DIAGNOSIS

DR. EDWARD L. YOUNG: Our problem is the diagnosis of a mass that is known to have existed for at least a year in a woman of sixty and to have grown during that period without affecting her general health or causing any subjective symptoms. The possibilities of a mass in that region come down to a definite number. The mass was apparently retroperitoneal and outside the gastrointestinal tract, according to the x-ray evidence. That leaves us with the possibility of a retroperitoneal tumor of lymphoid origin, a tumor coming from the left kidney or adrenal and a tumor of the pancreas. From the description, it should not have been from the liver, for instance an echinococcal cyst or an abnormal left lobe, and it should not have been from the spleen. The spleen was noted as being normal the previous year. I am sorry that there is no note in this record about whether the mass went through to the flank on palpation. This always suggests a kidney tumor. I think that the feel of a tumor such as this helps very much in connecting it with the kidney. Nothing abnormal was found in the urine. Moreover, there is no evidence of any study of the urinary tract, and we may therefore assume that the examiners were fairly sure that the mass was not renal in origin.

The question of pancreatic tumor comes up. The pancreas is a retroperitoneal fixed organ. When this mass was first felt, it was described as irregular but not movable. Of course the question of movability of a pancreatic tumor depends on the part of the pancreas from which it arises, and whether or not it is in contact with the liver, which must move on respiration. The commonest tumor of this size in the pancreas is, of course, a cyst, probably of the tail of the organ. It could move with respiration, but I must confess it is not usual.

Was it possibly a cyst of mesenteric origin? It could not be an omental cyst, of course, and make a defect in the posterior wall of the upper medial part of the stomach. I suppose it is possible for a cyst of the mesocolon to develop in such fashion as to make a defect as described in the x-ray report. That would be more freely movable than a pancreatic cyst.

Without getting any help from the x-ray findings, but merely going on what is given here, it is a little difficult for me to make a differential diagnosis between a cyst of the mesentery and a pancreatic cyst. Pancreatic cysts are very uncommon. Up to 1936,—I think I looked them up at that time,—there had been only 5 in sixteen years at the Massachusetts General Hospital. I believe the Mayo figures were more than 80 cases out of 750,000 patients, so that it is not common. Mesenteric cyst likewise is not common, and my belief is that they do not show themselves to be quite so large as this mass was. I should like to "stick my neck out" and say this is a pancreatic cyst first, in spite of the movability. Mesenteric cyst is second. I do not believe it is connected with the kidney or adrenal, and I do not believe it is connected with the liver. I should like to allow myself a chance to change my opinion after Dr. Holmes clears everything up.

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Dr. George W. Holmes: Unfortunately, the evidence that I have here does not clear anything up. As a matter of fact, all one can be certain about is that there is nothing wrong in the stomach. I should think the description would lead you to suspect that the man who examined the case thought the tumor was in the region of the pancreas.

Dr. Young: Of course the thing to do, if it is a pancreatic cyst, is to take it out if possible. Such cysts may be simple; they may be malignant. Even if they are simple, they may have to be marsupialized because of the impossibility of taking them out. If they are malignant, the effort should certainly be made to remove them.

Clinical Diagnosis

Carcinoma of the gall bladder.

Dr. Young's Diagnosis

Pancreatic cyst.

Anatomical Diagnosis

Papillary adenocystoma of the pancreas.

Pathological Discussion

Dr. Tracy B. Mallory: This patient was operated on by Dr. Claude E. Welch, who split the gastrocolic omentum and came immediately down on a cystic structure. He was at first unable to decide which organ it was attached to, but it proved fairly readily mobilizable, and when he brought it farther up into the wound it became clear that it was attached to the pancreas. He was able to remove it without too much difficulty, and then found that in doing so he had completely removed the middle section of the pancreas. He therefore went back and removed the distal fragment of the pancreas, to be on the safe side. This distal fragment was atrophied, and when it was cut across, a widely dilated pancreatic duct was found, with practically no recognizable pancreatic tissue. Microscopic sections showed total atrophy of the acinar cells, but the islands were perfectly preserved. It was exactly equivalent to the type of atrophy that develops from ligation of the pancreatic duct in an experimental animal. The cyst itself was 6 cm. in diameter and was multilocular, consisting of multiple cavities varying from pinpoint in size up to a centimeter or more in diameter. In a great many of these cavities, papillary projections were found, and we must classify this definitely as a neoplasm, a papillary adenocystoma of the pancreas. Whether it is benign or malignant is a little difficult to be sure of. We have seen one case of this sort, which Dr. Young perhaps remembers, since it was his originally, of frankly malignant papillary carcinoma of the pancreas. That recurred after a considerable interval, seven years, I believe. This tumor in comparison looks much less malignant. I think it is quite possible that the patient was cured, but I should not be surprised at a delayed recurrence.

Dr. Young: This interests me, because when you reviewed the slides of the original case you believed it was papillary cystadenoma and nonmalignant. It was first reported as malignant, and the patient did well and apparently was cured. It recurred six and a half years later, and she died seven and a half years after the original operation.

CASE 27232

Presentation of Case

A forty-three-year-old housewife entered the hospital complaining of abdominal pain.

The patient had felt perfectly well until one year before admission, when she noticed that she was becoming pale, rather weak, tired easily and was slightly dyspneic on exertion. No localizing symptoms appeared until three months before admission, at which time a sharp pain developed in the right upper quadrant of her abdomen, radiated to the right shoulder blade, and was aggravated by breathing and lying on her back. Shortly thereafter, the pain also included the epigastric region, and six weeks later it developed in the left lower quadrant, where it was stabbing in character and slightly increased by respiration. The pain became constant, and the patient went to bed suffering from anorexia and a considerable increase in exertional dyspnea. One month before admis-

sion, a loss in weight was first noticed and, in addition, an increase in the size of her abdomen. The husband believed the patient to be a little jaundiced, but no color change was noticed in the stools or urine. Two and a half weeks before admission, examination showed an enlarged liver and spleen. Gradually her dyspnea became more marked, and the right upper-quadrant pain exaggerated. One week before entry the patient was admitted to another hospital, where x-ray films were taken. At no time had there been nausea, vomiting, cough, urinary changes or vaginal bleeding. She had lost 20 pounds in weight.

The patient's father had died of carcinoma of the esophagus. The past illnesses were noncontributory.

On examination the patient was flushed and appeared chronically ill, and there was evidence of recent weight loss. The heart was normal, the blood pressure 130 systolic, 80 diastolic. At the left lung base, there were diminished excursion, slight percussion dullness and diminished breath sounds. The abdomen was distended and tympanitic, and an occasional peristaltic sound was heard. No shifting dullness was elicited. A tender edge, believed to be liver, was felt in the right upper quadrant and in the epigastrium. The spleen was not palpable, but percussion dullness over the region of the spleen could be made out. Rectal and pelvic examinations were negative.

The temperature was 99°F., the pulse 100, and the respirations 30.

The urine showed a + test for albumin, with an occasional white blood cell per high-power field and many bacteria in the sediment. The blood showed a red-cell count of 3,300,000 with a hemoglobin of 10.9 gm. (photoelectric-cell technic), and a white-cell count of 8600 with 82 per cent polymorphonuclears. A blood film showed considerable marrow activity with increased platelets, some shift to the left in the polymorphonuclears, stippled and polychromatophilic red cells and a few immature unidentified cells. The nonprotein nitrogen of the blood serum was 27 mg. per 100 cc.; the blood Hinton reaction was negative. The stools were normal.

X-ray films of the gastrointestinal tract taken in another hospital were interpreted as showing flattening of the greater curvature of the stomach due to pressure from what was believed to be an enlarged spleen. The stomach emptied in six hours; the colon was low and atonic. A barium enema revealed no significant findings. With a Graham test no dye entered the gall bladder. The genitourinary tract was normal.

A flat plate of the abdomen taken in this hospital showed a large collection of gas in the left mid-abdomen having the shape of the stomach antrum. There also appeared to be some gas-filled loops of small bowel in the mid-abdomen, but no dilated loops were visualized.

An electrocardiogram showed sinus tachycardia, low voltage in QRS, left-axis deviation and total inversion of Lead 3. T_1 and T_2 were tall and upright, and T_3 was inverted. Lead 4 was normal, save for low diphasic T waves.

On the third hospital day an operation was performed.

Differential Diagnosis

Dr. Leland S. McKittrick: It seems to me that the man who operated on this patient was a far better diagnostician than I am, or that he had some information I do not know of. I should not know what in the world to operate for. Here is a woman of forty-three, with pallor, weakness and slight dyspnea on exertion, who tired easily. Sometimes in carcinoma of the stomach or cecum there is such severe anemia that the patients get short of breath and have the other symptoms that go with inadequate oxygenation of the tissues. But that is not an outstanding surgical symptom. The patient was evidently not well for a long period, but nothing definite came into the picture until three months before admission, when she had sharp pain in the right upper abdomen radiating to the shoulder blade, aggravated by breathing and by lying on her back. I suppose that means something, but I cannot figure it out. Another point that is intriguing and confusing to me is that the pain became constant in the left lower quadrant, and that the patient went to bed suffering from anorexia and considerable increase in exertional dyspnea. She had had weight loss and possibly a little jaundice; there was no suggestion of it on physical examination. She had increase in the size of her abdomen. She is said to have had a palpable spleen two and a half weeks before admission, but x-ray films taken on the outside were essentially negative. I think it might be best to see the x-ray films now.

Dr. George W. Holmes: I am afraid that I am not going to help you. At first glance, one wonders how they could interpret this shadow as gas in the stomach. These films, I presume, were taken with the patient lying on her back. It is hard to tell. The striking thing is that there is no gas in the upper abdomen. One cannot see the diaphragm. If I could tell you whether the fundus of the stomach was displaced forward or backward, it would help a great deal in deciding whether the mass was liver or spleen. It must be either a very large liver or spleen or a very large mass.

DR. MCKITTRICK: In addition to what Dr. Holmes has said, we learn from the record that the patient had a positive Graham test. I am trying to find a surgical lesion, but not with much success. She may or may not have had gallstones. Certainly, they are not what she came into the hospital for. Apparently she had a large liver, and presumably a large spleen. That again is against a surgical lesion of a primary nature. The discomfort she had was certainly not characteristic.

In summary, we have a forty-three-year-old woman who had symptoms that went back a year, beginning with pallor, weakness, fatigue, and dyspnea on exertion. Three months before admission, pain came into the picture. The patient was distended, had supposedly a large liver and a large spleen, and her gall bladder did not fill. What this elaborate report on the blood means, I am ashamed to say, I do not know. I shall have to disregard it. The heart was normal on physical examination, and, Dr. Bland tells me, essentially normal in the electrocardiogram. Therefore, the dyspnea on exertion was probably not due to any heart abnormality. This woman, I believe, had either biliary-tract or neoplastic disease. It seems to me that neoplasm along the gastrointestinal tract has been reasonably well excluded by x-ray study. Carcinoma of the pancreas one might consider because of the steady constant pain that she had when she entered the hospital. The large spleen is not very satisfactorily explained on that premise, although I have seen large spleens from metastasis secondary to carcinoma of the pancreas. The distention, I suspect, was due to fluid in the abdomen, in addition to an excess of gas such as one sees in carcinomatosis or in cirrhosis. The rectal examination was negative. In other words, no nodule was felt in the pelvic floor. Somehow, I am inclined to believe that this may well not have been a carcinomatous mass with a carcinomatosis. I suppose one always has to consider, in the presence of unexplained abdominal findings, the question of Hodgkin's disease with involvement of the liver and of the spleen and possibly with retroperitoneal glands. I do not believe that the patient had a surgical lesion. I am going to put as my first impression cirrhosis of the liver, although there is nothing in the record to warrant any suggestion as to its etiology. The second guess that I can make would be a malignant lymphoma, and from there on it would be an open field.

DR. EDWARD L. YOUNG: Do you think peritoneoscopy would have helped?

DR. MCKITTRICK: I think it would have been a great deal of help.

DR. WILLIAM B. BREED: I should like to ask Dr. Richardson about the blood.

DR. WYMAN RICHARDSON: I looked at the blood. May I read my notes? I saw the patient a short time before the answer was discovered and made the following notes:

> The abdomen is very much distended and tympanitic. I cannot make out any large amount of fluid. There is no general glandular enlargement. Blood smear shows considerable marrow activity, with increased platelets, some shift to the left of polymorphonuclears; stippled and polychromatophilic red cells and a few very immature and unidentified cells are present. The clinical and blood picture, to me, rules out cirrhosis of the liver and Banti's disease (thrombosis of the splenic vein). The most probable diagnosis is malignant disease of some sort, with "myelophthisic" anemia most probable. Leukemia is not excluded. There is a question of intestinal obstruction. I have considered tuberculosis, but this is not likely. Further study should include a flat plate of the abdomen, peritoneoscopy and possibly bone-marrow biopsy if no definite diagnosis is established.

I might say I thought before this problem was answered that the patient had carcinoma of the pancreas, with metastases. I should like to add one word: A blood picture that shows this amount of marrow activity with immature red cells and immature white cells is not compatible with anemia from cirrhosis of the liver or even from hemorrhage. It means, then, some active marrow disease, and it is not infrequently seen in severe neoplasm, especially when the liver is very much involved.

CLINICAL DIAGNOSES

Malignant disease.
Myelophthisic anemia.

DR. MCKITTRICK'S DIAGNOSES

Cirrhosis of liver.
Malignant lymphoma.

ANATOMICAL DIAGNOSES

Carcinoma of gall bladder, with extension to liver and metastases to lung, hepatic, retroperitoneal and bronchial lymph nodes.
Pulmonary collapse, lower lobes, bilateral.
Ascites.
Arteriosclerosis, aortic and coronary, slight.

PATHOLOGICAL DISCUSSION

DR. TRACY B. MALLORY: I think possibly the statement in the record that operation was performed is misleading. The operation was peritoneoscopy. Dr. Edward B. Benedict is not here to describe his findings, but it was obvious at a glance that the liver was filled with metastases.

The patient rapidly failed and died. At the time of autopsy, the entire upper abdomen was filled with liver. There were 5 kilograms of it. The spleen was not significantly enlarged, weighing 270 gm., which is not palpable enlargement. The particular portion of the liver that was most enlarged was the left lobe, and it was unquestionably that which was felt and interpreted as the spleen. The enlargement of the left lobe I am sure was quite sufficient to account for the abnormality on x-ray examination. The gall bladder at first glance seemed normal, although a little dilated. The anterior wall was thin. When it was cut into, it contained a large amount of clear, colorless fluid. On the posterior wall, in the bed adjacent to the liver, was a fungating cauliflower mass. This unquestionably was a primary carcinoma of the gall bladder that extended directly into and almost completely replaced the liver. The amount of liver parenchyma left was under 500 gm., I should think.

DR. MCKITTRICK: Dr. Holmes really gave away what he had in the back of his mind. He gave me quite a tip-off when he stressed the density in the upper abdomen, because it would be quite hard to explain the combination of that density with the location of the gas bubble on any other basis. Do you ever get as large a liver as that in either cirrhosis or lymphoma?

DR. MALLORY: Yes; in both. Five kilograms of liver are not extremely rare in early stages of alcoholic cirrhosis.

DR. MCKITTRICK: Do you usually get a diffuse enlargement, or is it apt to be more or less localized to one lobe?

DR. MALLORY: That is unusual in cirrhosis, but is certainly not uncommon in cancer.

DR. MCKITTRICK: I think I should have done better with Dr. Holmes's interpretation of the x-ray films.

DR. RICHARDSON: And the blood smear.

DR. HOLMES: If you could have been sure that the fundus of the stomach was displaced backward instead of forward, you could be certain it was liver and not spleen.

DR. MALLORY: I agree with Dr. Richardson's point. The blood picture was an excellent lead.

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THE CLOSED-STAFF HOSPITAL

It was not very long ago — about the turn of the century — when those members of the public who required more than office care from their physicians or surgeons turned away with suspicion whenever hospital care was suggested. This attitude, doubtless, was only a later expression of the justifiable fear that existed in the "Sairy Gamp" era when hospitals were either poorhouses or institutions for the insane and those suffering from chronic alcoholism. Brought up to date, this fear expressed itself in terms of dread of "unnecessary cutting," "experimentation by students" and the like. It forced the members of the medical profession to compromise their ideals and to care for their major obstetric, medical and surgical problems in private homes, pending education of the public to the advantages of hospitalization. Thanks to the advancement in the science as well as the practice of medicine, the increased use of hospitals as teaching centers, the development of new ideas in the management and training of the house staffs in the hospitals but, most of all, to the mental acuity of the patients and their families, this education was sufficiently far advanced so that hospitalization was not only accepted but demanded by seriously ill patients at the time of the outbreak of World War I.

With this increased use it was shortly apparent to the profession that there were illegitimate as well as legitimate advantages to having a hospital to call on. Such evils as therapy — particularly surgical — without diagnosis, inadequate and incompetent medical care, the blocking rather than the facilitation of post-mortem examinations, the neglect of records, with resulting medicolegal complications and injustices, and many unethical financial arrangements between unscrupulous physicians and surgeons became commonplace and were rapidly undoing all the educational good that had been accomplished with so much effort.

Some disciplinary measures were essential. Because the surgeon had the greater and more dramatic opportunity to fall by the wayside, corrective action was first taken by this branch of the profession. This led to the formation of the American College of Surgeons. Over the intervening years since its organization, this and other societies — backed by the financial support of an enlightened public — have evolved a method whereby a maximum of control is exercised over those persons and tendencies in the medical profession that consciously or unconsciously threaten to bring back the evils mentioned above. This has been accomplished by keeping the services rendered by both the hospitals and the visiting staffs at the standard that is acceptable to the majority of doctors. Such hospitals as meet these standards are rewarded by certification of acceptability. This is inevitably followed by an improvement in the caliber of their resident staffs, an easing of their financial burdens through willingness of patients to pay more and promptly,

and an encouragement to their trustees in obtaining public support for their efforts to protect the local communities.

Furthermore, this certification leads to the requirement of the hospital that the work and medical morals of the visiting staff be kept at a high level. To accomplish this the hospitals — for their own self-protection — have created the closed-staff and courtesy-staff organization and denied to such members of the medical profession as were either unwilling or unable to conform to the minimum standards set up by the American College of Surgeons and other analogous institutions the right to practice or care for patients within their walls. Those physicians and surgeons who are allowed membership on such closed or courtesy staffs are universally favorable to the arrangement and rightly jealous of their professional and ethical standards. In the light of the present-day attitude of the public, as represented by their financial support of such hospitals, by their patronization of such staff members and by their demand for such facilities in cases of serious illness, it is apparent that this movement meets with the approval of the intelligent part of the patient population.

Physicians and surgeons who have not been granted these privileges are prone to cry favoritism, graft in high places, coercion and so forth. They either ignore or know nothing of the historical background that led to the present-day arrangement. In particular they fail to recognize that any member of the medical profession, regardless of the school from which he graduated or the societies to which he belongs, who can demonstrate to fellow members in his community, and to the trustees of the hospital that serves his community, that he is technically equipped, adequately trained, ethical and desirous of keeping constantly up to date in his profession will have no difficulty in obtaining permission to practice in his local hospital, even though it is inspected and certified as meeting the minimum requirements of the American College of Surgeons. They must not forget that such certification has the actual or implied support of the American College of Physicians, the American Hospital Association, the American Nursing Association, the American Red Cross and similar organizations. Attempts to camouflage inadequacy, incompetence or lack of ethics under the specious plea that membership in a state medical society automatically negates the considered judgments of the doctors' peers are doomed to failure and are indefensible.

X-RAY EXAMINATION OF RECRUITS

It seems quite clear from the article on "Tuberculosis and Mobilization" in this issue of the *Journal* that the National Tuberculosis Association has made significant recommendations regarding the elimination of tuberculosis in those selected for service in the forces of the United States. It has recommended that Washington order x-ray examination of the lungs to be carried out by the local selective-service boards, thus rooting out tuberculosis at the source, with a consequent saving of time and money. Secondly, it points out that if examination is put off until the appearance of the candidate before the induction board, enrollment into the service should be delayed until the result of the examination is known. Both recommendations are sound.

It is pertinent to consider what x-ray technic is best suited for such a survey of recruits. Miniature films are becoming increasingly popular in mass-survey work. The 35-millimeter and 4-by-5-inch films are both photographic reproductions of the image thrown on a fluoroscopic screen, and the procedure is known as fluorography. The initial cost of equipment is high, but the cost per picture very low,[1] being at least one tenth that of the standard 14-by-17-inch film. But factors other than expense influence the decision of the best technic.

It has recently been shown that in carefully studied series of x-ray examinations 4-by-5-inch films failed to reveal 2.6 per cent of the cases of tuberculosis diagnosed by means of standard films.[2, 3] In a survey of a million recruits, assuming the incidence of tuberculosis to be 1.0 per cent, examination by the miniature film on this

basis would fail to show 260 small lesions in the lung. The small lesion that is unrecognizable by physical examination presumably represents active tuberculosis, and is therefore potentially a source of danger to the candidate as well as to those associated by contact with him. Further research will undoubtedly perfect the accuracy of the miniature film, but so long as an error of 2.6 per cent persists in the hands of competent observers its adoption as a weeding-out procedure does not seem justified.

Spillman[4] has shown how the eventual cost of missed cases of tuberculosis in World War I has mounted to hundreds of millions of dollars. Since standard x-ray films remain the final word in the diagnosis of pulmonary disease not detectable by the usual physical examination and since most radiologists are not familiar with the interpretation of the miniature reproductions, the chest examination of all recruits by means of 14-by-17-inch films cannot be too strongly urged, in spite of the apparent economy of miniature films.

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2. Potter, H. E.; Douglas, B. H. and Birkelo, C. C. The miniature x-ray chest film. *Radiology* 34:283-291, 1940.
3. Douglas, B. H. and Birkelo, C. C. The miniature x-ray film of the chest. *Am. Rev. Tuberc.* 43:108-116, 1941.
4. Spillman, R. The value of radiography in detecting tuberculosis in recruits. *J. A. M. A.* 115:1371-1378, 1940.

MEDICAL EPONYM

Hoffmann's Anodyne

Originally one of the secret remedies that Friedrich Hoffmann (1660-1742) dispensed for a consideration, this mixture gradually became a universal pharmacopoeial and popular medicine. The following translated quotation is from the second edition of Hoffmann's *Medicinae Rationalis Systematicae* [*Theory and Practice of Medicine*] (Vol. III, Sect. ii, p. 533. Frankfurt, 1738), "wherein are set forth the true fundamentals of therapy, the process of healing, laws of nature and of medical science, as well as select remedies . . .":

> To be sure, I too have resorted fairly frequently to the use of correct opiates. But ever since the fortune of heaven bestowed on me the discovery of this penetrating and pleasant-smelling liquid,—with its aromatic taste and odor, formed from a portion of vitriol of sulfur (which, indeed, was used even by chemists of old as an anodyne), by a special chemical formula of preparation,—I have refrained from all others. Now this liquid, which I am accustomed to denote by the name of liquid mineral anodyne, is formed from sulfur alone. It burns rapidly and fiercely and is consumed, and catches fire very quickly from the flame of a candle even when held away from it a distance of three fingers, and in a warm room it evaporates speedily; yet to the touch it is very cold, just like ice, and when thoroughly distilled and purified it floats on the top of water, just like oil. The uses of this remedy are many, and its virtues varied: it is admirable for soothing pain and inducing slumber, and it is therefore used with great advantage in sharp attacks of colic, stone, cardialgia, gout or pains of head and teeth. It also starts perspiration, and although it is very heating, it does not stir up the blood. Moreover, it leaves no feeling of torpor or weakness in the head; for that reason it can be given with benefit to all invalids when their strength is at a low ebb, as in a hectic fever, and what is even more surprising, with an actual increase in their strength. Finally, because its action is first and foremost on the stomach,—in all stomach disorders, nausea, inflation, hypochondria, asthma and cardialgia,—it shows unequaled effectiveness in putting an end to flatus.

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

SECTION OF OBSTETRICS AND GYNECOLOGY*

Raymond S. Titus, M.D., *Secretary*
330 Dartmouth Street
Boston

Ectopic Pregnancy With Fatal Termination

A thirty-six-year-old primipara began to flow thirty-five days after a normal period and flowed for only two days. It was thought that her period was shortened because the patient's feet had become wet. Three days after the flow ceased, she had a severe pain in the lower abdomen, which caused her to perspire freely. She was seen by her family physician.

Examination revealed a temperature of 99.3°F., a pulse of 60 and a blood pressure of 125 systolic, 70 diastolic. The abdomen was soft and nontender. The pain was attributed to menstrual discomfort, and morphine was prescribed. Four hours later, the pain in the lower abdomen had subsided, but there was acute pain in the epigastrium. The temperature at this time was 96.4°F., the pulse 60, and the blood pressure again 125 systolic, 70 diastolic. A telephone conversation four hours later revealed that the patient had vomited and felt much better. She was seen again in four hours, when her pulse was rapid and she was in a serious condition. She was taken to the hospital by ambulance and died on arrival. Post-mortem ex-

*A series of selected case histories by members of the section will be published weekly. Comments and questions by subscribers are solicited and will be discussed by members of the section.

amination revealed rupture of the left tube and much free and clotted blood in the pelvis and abdomen.

Comment. This case emphasizes the importance of appreciating that scanty flow with abdominal pain occurring any time after the expected menstrual date may mean disease and should suggest the possibility of ectopic pregnancy. This indicates immediate pelvic examination. No vaginal examination is reported to have been made in this case. It is really inexcusable that when this patient was first seen the necessity for a vaginal examination did not become apparent. Undoubtedly had one been made, tenderness in the pelvis would have led to earlier operation. It is also difficult to believe that, in view of the amount of blood that was subsequently found in the abdomen, the initial pain in the lower abdomen, so severe as to cause perspiration, was not accompanied by tenderness and spasm. There is no medical excuse for this mistaken diagnosis and subsequent fatality.

DEATH

DOUGHERTY — HARRY L. DOUGHERTY, M.D., of Boston, died June 1. He was in his forty-third year.

Dr. Dougherty received his degree from the University of Louisville School of Medicine in 1925. He was a member of the Massachusetts Medical Society and the American Medical Association.

He is survived by his widow, his parents, two daughters, two sons, four sisters and three brothers.

MISCELLANY

SEROLOGIC TESTS FOR THE DIAGNOSIS OF SYPHILIS AND GONORRHEA

The Health Department of the City of Boston has announced that, effective June 1, the routine serologic test at the Bacteriological Laboratory for the diagnosis of syphilis will be the Hinton flocculation test. Temporarily, on request, parallel spinal-fluid and blood Wassermann tests will also be carried out. The Kahn test will be performed only when requested.

NOTE

At a meeting in Richmond, Virginia, on May 5, the American Branch of the International League against Epilepsy elected Dr. H. Houston Merritt, of Boston, president, and Dr. Frederic A. Gibbs, of Boston, secretary-treasurer, for the ensuing year.

CORRESPONDENCE

QUALIFICATIONS FOR HOSPITAL-STAFF MEMBERSHIP

To the Editor: My attention has been called to several instances in which members in good standing in our society have been refused courtesy privileges in certain hospitals. In each case the physician concerned was a graduate of a school other than Class A, according to the usual standard of classification.

The reason invariably set down for the refusal to grant such privileges is that the American College of Surgeons will not certify hospitals if graduates of such schools are admitted to their staffs.

There is within this state an ever-increasing group of these graduates who have been found qualified by the Massachusetts Board of Registration in Medicine, who have been considered capable and conscientious by the boards of censors of the Massachusetts Medical Society and who practice good medicine. This denial of hospital privileges has in specific instances not only made the paths of practice difficult for these doctors, but has brought about actual hardship, and does not seem just to me.

I am quite aware of our lack of jurisdiction over the action of the staffs of hospitals. Nevertheless I do question the wisdom of tacitly permitting practices which may at some time be held to be discriminatory, hence damaging, to exist within our membership.

When it is considered that such action as is taken is in compliance with the rule of the American College of Surgeons and that the burden is placed upon the hospital, I sometimes wonder just what the advantages of hospital membership in the college are. All this quite naturally raises the questions from whom the American College of Surgeons derives its authority and whether or not the pursuance of policies which might one day be held to be discriminatory upon the part of our membership is ethical under the standards set up by our society.

FRANK CRUICKSHANK, M.D.

1247 Beacon Street
Brookline, Massachusetts

NOTICES

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

A program in public-health engineering, covering military and public-health practice, will be given at the Department of Biology and Public Health, Massachusetts Institute of Technology from June 16 to July 25; the program will emphasize the application of facilities in public-health engineering to industrial and military problems of the national defense preparation. Basic training in chemistry and biology is required for this program, which is intended primarily for graduate engineers, sanitary chemists and biologists, bacteriologists, officers in the United States military service and others engaged in public-health engineering work.

EVANS AUDITORIUM

The third of a series of lectures by Dr. Albert B. Ferguson on "Roentgenology of the Bones and Joints" will be delivered at Evans Auditorium, 78 East Concord Street, Boston, on Monday, June 9, at 7:30 p.m.

The medical profession is invited.

AMERICAN COLLEGE OF PHYSICIANS

The twenty-sixth annual session of the American College of Physicians will be held in St. Paul, Minnesota, on April 20–24, 1942. Dr. Roger I. Lee, of Boston, president of the American College of Physicians, will have charge of the program of the general sessions and lectures. Dr. John A. Lepak, of St. Paul, has been appointed general chairman; he will be in charge of the program of hospital clinics and round-table discussions,

as well as local arrangements. Mr. Edward R. Loveland, executive secretary of the college, 4200 Pine Street, Philadelphia, will have charge of the general management of the session and of the technical exhibits.

AMERICAN CONGRESS OF PHYSICAL THERAPY

The twentieth annual scientific and clinical session of the American Congress of Physical Therapy will be held September 1–5, at The Mayflower, Washington, D. C. Mornings will be devoted to the annual instruction course, and afternoons and evenings to scientific sessions. The seminar and convention proper will be open to physicians and qualified technicians.

For information concerning the seminar and preliminary program of the convention proper, address American Congress of Physical Therapy, 30 North Michigan Avenue, Chicago.

At the same time, the twenty-fifth annual meeting of the American Occupational Therapy Association will be held at The Mayflower. A combined meeting will be held on Wednesday, September 3. For information concerning the American Occupational Therapy Association, address Mrs. Meta R. Cobb, 175 Fifth Avenue, New York City.

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UNITED STATES CIVIL SERVICE EXAMINATIONS

Public Health Nursing Consultant, $2600 to $3000 a Year
Medical Technician, $1620 to $2000 a Year
Junior Laboratory Helper, $1440 a Year

The United States Civil Service Commission has announced open competitive examinations to fill the positions of public-health nursing consultant, medical technician and junior laboratory helper in the United States Public Health Service of the Federal Security Agency. Full information regarding the qualifications required and the applications for these examinations may be obtained from the Secretary, Board of United States Civil Service Examiners, at any first-class or second-class post office, or from the United States Civil Service Commission, Washington, D. C.

EXAMINATIONS FOR APPOINTMENTS IN THE MEDICAL CORPS OF THE UNITED STATES NAVY

The next examination for appointments as assistant surgeon (lieutenant, junior grade), United States Navy Medical Corps, will be held at all major Medical Department activities on August 11 to 15, inclusive. Applications for this examination must be received at the Bureau of Medicine and Surgery, Navy Department, Washington, D. C., not later than July 15.

Applicants for appointment as assistant surgeon must be citizens of the United States, more than twenty-one but less than thirty-two years of age at the time of acceptance of appointment, and graduates of a Class A medical school who have completed at least one year of intern training in a hospital accredited for intern training by the Council on Medical Education and Hospitals of the American Medical Association.

A circular of information listing physical and other requirements for appointment, subjects in which applicants are examined, application forms and other data pertaining to salary, allowances and so forth may be obtained from the Bureau of Medicine and Surgery on request.

An examination for appointment as acting assistant surgeon for intern training in naval hospitals accredited for intern training by the Council on Medical Education and Hospitals of the American Medical Association will be held at all major Medical Department activities on June 23 to 26, inclusive. Students in Class A medical schools who will complete their medical education this year are eligible to apply for these appointments, and if successful will receive their appointments approximately one month after the date of the examinations. Students in Class A medical schools who will have completed their third year of medical education this year are eligible to take this examination, and if successful will receive their appointments on or about July 1, 1942, after they have completed their medical education.

Applicants for appointment as acting assistant surgeon for intern training must be citizens of the United States, more than twenty-one but less than thirty-two years of age at the time of acceptance of appointment. Acting assistant surgeons are appointed for a period of eighteen months. After the appointee has served as an intern in a naval hospital for twelve months, he is eligible for and may take the examination for appointment as assistant surgeon.

A circular of information listing physical and other requirements for appointment as acting assistant surgeon, subjects in which applicants are examined, application forms and so forth may also be obtained from the Bureau of Medicine and Surgery on request.

Assistant surgeons and acting assistant surgeons for intern training are appointed in the rank of lieutenant (junior grade), United States Navy Medical Corps. The pay and allowances for an officer of this rank total $2699 per year if he has no dependents, and $3158 per year if he is married or has dependents.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, June 8

Monday, June 9

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

*7:30 p.m. Roentgenology of the Bones and Joints. Dr. Albert B. Ferguson. Evans Auditorium. 78 East Concord Street, Boston.

Tuesday, June 10

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

Wednesday, June 11

*12 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

June 8–9 — American Psychopathological Association. Hotel Traymore, Atlantic City, New Jersey.

June 16–July 25 — Massachusetts Institute of Technology. Page 996.

June 22–24 — Maine Medical Association. Marshall House, York Harbor, Maine.

September 1–5 — American Congress of Physical Therapy. Notice above.

September 1–5 — American Occupational Therapy Association. The Mayflower, Washington, D. C.

October 13–24 — 1941 Graduate Fortnight of the New York Academy of Medicine. Page 834, issue of May 8.

October 14–17 — American Public Health Association. Page 579, issue of March 27.

April 20–24, 1942 — American College of Physicians. Page 996.

District Medical Society

NORFOLK SOUTH

June 11 — Page 961, issue of May 29.

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Roentgen Interpretation. By George W. Holmes, M.D., roentgenologist, Massachusetts General Hospital, and clinical professor of roentgenology, Harvard Medical School; and Howard E. Ruggles, M.D. Sixth edition, thoroughly revised. 8°, cloth, 364 pp., with 246 illustrations. Philadelphia: Lea and Febiger, 1941. $5.00.

Lectures on Diseases of Children. By Sir Robert Hutchison, Bart., M.D., LL.D., F.R.C.P., consulting physician, London Hospital and Hospital for Sick Children, Great Ormond Street; and Alan Moncrief, M.D., F.R.C.P., physician to the Children's Department, Middlesex Hospital, and to outpatients, Hospital for Sick Children, and pediatrician, Queen Charlotte's Maternity Hospital. Eighth edition. 8°, cloth, 471 pp., with 107 illustrations. Baltimore: Williams and Wilkins Company, 1940. $6.75.

Introduction to Physical Biochemistry. By J. M. Johlin, Ph.D., D.Sc., associate professor of biochemistry, Vanderbilt University School of Medicine. 8°, cloth, 231 pp., with 10 illustrations. New York: Paul B. Hoeber, Incorporated, 1941. $2.75.

Health in Iceland. By Vilmundur Jónsson, director of public health, Iceland. A reprint from *The Report on Public Health in Iceland, 1938.* 8°, paper, 29 pp., with 3 charts and 1 map. Reykjavík: Ríkisprentsmidjan, 1941.

Physical Medicine: The employment of physical agents for diagnosis and therapy. By Frank H. Krusen, M.D., associate professor of physical medicine, Mayo Foundation, University of Minnesota, and head of Section on Physical Therapy, Mayo Clinic. 8°, cloth, 846 pp., with 351 illustrations. Philadelphia: W. B. Saunders Company, 1941. $10.00.

A Short History of Psychiatric Achievement, with a Forecast for the Future. By Nolan D. C. Lewis, M.D., professor of psychiatry, College of Physicians and Surgeons, Columbia University, and director, New York State Psychiatric Institute and Hospital. 8°, cloth, 276 pp. New York: W. W. Norton and Company, Incorporated, 1941. $3.00.

Handbook of Anaesthetics. (Formerly by Ross and Fairlie.) Revised by R. J. Minnitt, M.D. (Liverpool), D.A. (D.C.P. and S. Eng.), lecturer in anesthesia, University of Liverpool, director of anesthetics, David Lewis Northern Hospital, Liverpool, and honorary anesthetist, Liverpool Royal Infirmary and Liverpool Maternity Hospital. With chapters on local and spinal anesthesia by W. Quarry Wood, M.D., Ch.M., F.R.C.S.E., surgeon, Edinburgh Royal Infirmary. Fifth edition. 12°, cloth, 364 pp., with 103 illustrations. Baltimore: Williams and Wilkins Company, 1940. $4.00.

Hutchison's Food and the Principles of Dietetics. Revised by V. H. Mottram, M.A. (Cant.), professor of physiology, King's College of Household and Social Science, University of London; and George Graham, M.D. (Cant.), F.R.C.P. (Lond.), physician to St. Bartholomew's Hospital. Ninth edition. 8°, cloth, 648 pp., with 30 illustrations. Baltimore: Williams and Wilkins Company, 1940. $6.75.

BOOK REVIEWS

Surgery of Modern Warfare. Vol. 1. By sixty-five contributors. Edited by Hamilton Bailey, F.R.C.S. 4°, cloth, 480 pp., with 502 illustrations. Baltimore: Williams and Wilkins Company, 1941. $10.00.

This is a very timely book, and will find great usefulness in training the medical personnel of our army and navy in the methods of traumatic surgery. It is written by sixty-five specialists who have had first-hand experience with the casualties of the war in England. The first part of the book is devoted to general subjects such as burns, septic wounds, prevention of tetanus and skin grafting; the second half deals with wounds in the various organs and regions of the body. The difficult problems of traumatic neurosurgery are not considered but are to be the subject of a second volume.

If a generalization on such a detailed work as this is permitted, one would say that the great advances in the present war are the routine débridement of fresh wounds, and the use of closed plaster in the treatment of compound fractures that are accompanied by widespread destruction of soft tissue. The principle that the body will handle infection in very large wounds, if allowed to do so by immobilization and closed dressing, is associated in this country with the name of Winnett Orr and in Europe with Trueta. The substantiation of this work by such a critical writer as Bailey makes it obligatory that it should be adopted in this country by all those who are called on to do war surgery.

The certainty of active immunization for tetanus is not upheld by these authors as a proved fact. They use prophylactic antitoxin whether or not a patient has had toxoid previously. This contradicts American opinion, which considers active immunity to tetanus as a very reliable procedure. The authors record a definite clinical impression about the value of x-ray in the treatment of gas gangrene. No figures are given to prove this conviction, but the impression is so favorable as to warrant its use routinely.

The book has dozens of good illustrations, some of them done in color. This would be a monumental effort during peacetime. That it was produced by busy and harassed surgeons on war duty is a great compliment to their endurance and devotion to science.

An Introduction to Dermatology. By Norman Walker, Kt., M.D., LL.D., consulting physician; and G. H. Percival, M.D., Ph.D., physician for diseases of the skin, Royal Infirmary, Edinburgh. Ten edition. 8°, cloth, 391 pp., with 102 plates and 96 illustrations. Baltimore: Williams and Wilkins Company, 1939. $7.00.

This small book on dermatology has numerous interesting features. The senior author, a British dermatologist of wide experience, always writes in a very personal way and delves into his past contacts with patients for many apt cases and therapeutic results. He explains the derivations of many disease names, and other such bits of information are of interest to the reader. The descriptions of disease manifestations are not so profuse as those in many textbooks, but the excellent color plates provide the student with a lifelike appearance of many skin diseases. Many types of dermatitis are quite thoroughly discussed. Therapeutic measures are based on many years' experience in clinics and private practice, and often form an interesting contrast with the usual methods in this country. Syphilis is very inadequately handled.